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PREFACE TO THE THIRD EDITION.

The issue of the Eighth Decennial Revision of the United States Pharmacopœia as well as the general advance of scientific pharmacy have rendered necessary a new edition of this Treatise on Pharmacy in order that it may reflect its subject to date both in its official and practical aspects. Much new matter has been introduced and a large part of the text has been entirely rewritten.

As indicated in the Preface to the first edition, this book is not intended to take the place of the Pharmacopœia, but to serve primarily as an explanatory guide to the study and use of the official standard, which is necessarily confined to brief statements presuming prior knowledge for their comprehension. This is more than ever true in the case of the new Pharmacopœia, owing to its increased demands for standardization of botanical drugs, volatile oils and galenical preparations. These and other changes have made necessary a more elaborate explanation of the official requirements and tests, without which an intelligent use of our national standard would be impossible. To students and pharmacists alike such explanations should be welcome on account of the more rigid examinations now given by the Boards of Pharmacy, and the enforcement of pharmacy laws in conformity with the requirements of the Pharmacopœia.

The general plan of the book remains as originally outlined, as the author has been repeatedly assured by professional friends that it serves a good purpose. No effort has been spared to extend its scope and add to its usefulness. As heretofore the author's endeavor has been to supply a text-book which, while sufficiently comprehensive to serve as a trustworthy guide, should be devoid of all unnecessary material. It embodies his own experience extending over thirty-five years of a busy life as a practical pharmacist, as well as the fruits of the long continued labors of many able men both in this country and Europe to which the present advanced state of pharmacy is due.

The subjects treated in this book have been grouped under three distinct headings.

Part I. comprises General Pharmacy, which includes the study of weights and measures, specific gravity, the application and control of heat, mechanical subdivision of drugs, and methods of solution and separation, together with a classification and description of the various plant-products and solvents used in pharmacy.

Part II. treats of Practical Pharmacy. This involves a study of the official galenical preparations, together with the many operations of the dispensing-counter. It has been the author's aim to explain as clearly as possible the various processes and apparatus met with in this department, and to point out the difficulties likely to be encountered, as well as the remedies therefor. All suggestions made have been tried and verified by the author before offering them, so that statements made are based on actual experience.

Part III. is devoted to Pharmaceutical Chemistry, the study of which is of paramount importance to every pharmacist. While the subject is a very comprehensive one, and undoubtedly entitled to an extensive treatise, it has been confined, in this work, to such compounds as are either officially recognized in the United States Pharmacopœia, or are of special interest to pharmacists.

By a careful analysis of the working formulas of the Pharmacopœia it has been thought possible to render that excellent book more useful to students as well as pharmacists in general. The object constantly in view is to answer, if possible, the many questions of why and wherefore with which students and practising pharmacists are almost daily confronted. To what extent the writer has been successful in this direction must be left to the judgment of the pharmaceutical profession. He is fully aware that imperfections must of necessity exist in a work covering so extended a field of study, and he hopes that those better able to judge will kindly inform him of any apparent or real defects, so that they may be rectified in a future edition.

C. C. Jr.

Baltimore, 1906.

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PART I.

GENERAL PHARMACY.

CHAPTER I.

PHARMACOPŒIAS.

ALTHOUGH the term *Pharmacopœia* (from the Greek φάρμακον, medicine, and ποιεῖν, to make) is defined by lexicographers as meaning a book of formulas or directions for the preparation of medicines, the word has now received a more liberal construction, and is taken to include, besides the foregoing, also descriptions of vegetable as well as mineral and animal drugs, together with appropriate tests for establishing the identity and quality of the same, the whole prepared by some recognized authority.

The necessity for a definite and authoritative standard in the selection and preparation of medicines was long since recognized by all civilized nations; thus the London Pharmacopœia was established in 1618, that of Paris in 1639, and that of Edinburgh in 1699. The first truly national standard was that of France, issued in 1818, which retained the name of its predecessor, the Paris Pharmacopœia, and is even to-day still known as the Codex Medicamentarius. The first United States Pharmacopœia was established in 1820, prior to which time various foreign pharmacopœias had been in use in this country. The British Pharmacopœia, into which were merged the London, Edinburgh, and Dublin (established 1807) Pharmacopœias, was first issued in 1864; while Germany did not adopt a national standard until 1872, nearly two years after the restoration of the German empire. Owing to the rapid advances in the science of medicine and pharmacy, frequent revisions have become necessary, and the following table shows the dates of the last revised editions of the pharmacopœias of leading nations.

Country.	Date of Issue.
United States	1905
Switzerland (to be issued)	1905
Russia	1903
Italy	1903
Netherlands (Supplement)	1903
Japan (Supplement)	1902
Germany	1900
Sweden	1900
Austria (Supplement)	1900
Great Britain	1898
Denmark (Supplement)	1898
Norway	1895
France (Supplement)	1895
Denmark	1893
Roumania	1893
Japan	1891
Mexico (Supplement)	1890
Austria	1889
Netherlands	1889
Hungary	1888
Belgium	1885
Finland	1885
France	1884
Mexico	1884
Spain	1884
Portugal	1876

The Pharmacopœia of the United States, although without the power of legal enforcement by act of Government, is, nevertheless, recognized as an authority by the courts, and is the standard employed in the purchase of medical supplies for the Army and Navy of the United States. In some of the States it has been adopted as the legal standard in the enforcement of pharmacy laws, and this plan is likely to be followed by others. The Pharmacopœia as now published represents the joint work of the medical and pharmaceutical professions; but in the early part of the last century, when pharmacy had not yet reached the state of a fully developed profession in this country, the apothecary held a rather subordinate position, and therefore had no voice in the compilation of the first national Pharmacopœia, which was adopted in 1820 by a convention of physicians assembled at Washington, D. C., under the presidency of Dr. S. L. Mitchill, the publication of the book being entrusted to a special committee, of which Dr. Lyman Spalding was chairman, and both the Latin and English languages being used in the text. In 1830, through some misunderstanding and consequent dissatisfaction, two separate conventions were held for the revision of the Pharmacopœia, one in New York and one in Washington, and at the latter the Government medical service was represented for the first time and participated in the proceedings; at this time provision was also made for regular subsequent revisions every ten years. Owing to this confusion two distinct Pharmacopœias were published, one in 1830 in New York City, bearing the imprint "By the authority of the General Convention for the Formation of the American Pharmacopœia, held in 1830;" the other, published by authority of the National Medical Convention held at Washington, A. D. 1830, was issued in Philadelphia in 1831. In the Pharmacopœia of 1840 the Latin version of the text was omitted, and in this revision material aid was also given by the pharmacists, although they had no representation in the convention; numerous improvements in the working formulas appear in this edition. In the convention of 1850 two colleges of pharmacy were duly represented by delegates, and from this time forward the value of pharmaceutical collaboration has been recognized, and its influence is discernible in the many practical details of the Pharmacopœia. Since 1850 the convention for the revision of the Pharmacopœia has assembled in the city of Washington, D. C., regularly in the month of May of every tenth year; all duly incorporated medical and pharmaceutical societies and colleges throughout the United States are entitled to representation by three delegates, the three branches of the Government medical service being also represented by one delegate each. The final revision of the Pharmacopœia, under instructions from the convention, is entrusted to a committee of twenty-five members, who formerly also had charge of the publication of the book. In May, 1900, the national convention for the eighth decennial revision of the United States Pharmacopœia met in Washington, D. C., under the presidency of Dr. H. C. Wood, of Philadelphia, who had successfully guided the deliberations of the previous convention, in 1890. Among the important resolutions adopted at this meeting were one for the incorporation of the assembled body under the name of "The United States Pharmacopœial Convention," and another for the introduction into the Pharmacopœia of average approximate doses, to be stated after each pharmacopœial article. The business management and control of the affairs of the Convention, including the publication of the Pharmacopœia, have been placed in the hands of a board of trustees, composed of five men, of which Chas. E. Dohme, of Baltimore, Md., is the present chairman. The present Committee of Revision is composed of eleven physicians (of whom, however, only six are engaged in the practice of medicine) and fourteen pharmacists and chemists. Dr. Charles Rice, who had so ably filled the position of chairman of the Committee of Revision during the last twenty years, was again elected chairman in 1900, and served until his death, May 13, 1901. Since then Joseph P. Remington has been chairman.

As the Pharmacopœia is in almost daily use by the pharmacist, a short study of its plan and arrangement is desirable for a more intelligent understanding of the text. The titles of all drugs recognized in the Pharmacopœia, whether derived from the vegetable, mineral, or animal kingdom, are conveniently given in three subdivisions, known as the *official Latin name*, the *official English name*, and the *official definition*, to which is added an official description, by means of which the identity of all official substances can be readily established. The following examples will serve to illustrate the arrangement of pharmacopœial subjects:

SODII ARSENAS.	(Official Latin name.)
SODIUM ARSENATE.	(Official English name.)
$Na_2HAsO_4 + 7H_2O = 309.84$.	(Official definition.)
It should contain in an uneffloresced condition not less than 98 per cent. of pure di-sodium-ortho-arsenate, $AsO(OH)(ONa)_2 + 7H_2O$.	(Purity rubric.)
Colorless, transparent, monoclinic prisms, odorless, and having a mild, alkaline taste; caution should be used in tasting this salt, as it is very poisonous. Efflorescent in dry air, and somewhat deliquescent in moist air. Soluble in 1.2 parts of water at 25° C. (77° F.), and very soluble in boiling water; very sparingly soluble in cold, but nearly insoluble in boiling alcohol. When gently heated the salt loses 5 molecules of water (28.8 per cent.), and is converted into a white powder. At 148° C. (298.4° F.) it loses all of its water of crystallization; at a higher temperature it fuses, and at a red heat it is converted into pyroarsenate. Sodium arsenate should respond to the tests of identity and purity prescribed under Sodii Arsenas Exsiccatus.	(Official description.)

PODOPHYLLUM.	(Official Latin name.)
PODOPHYLLUM.	(Official English name.)
The dried rhizome of *Podophyllum peltatum*, Linné (Fam. *Berberidaceæ*).	(Official definition.)
Of horizontal growth and variable length, subcylindrical, flattened above, sometimes branched, consisting of joints 5 to 10 Cm. long, the internodes 2 to 8 Mm. thick; externally pale yellowish-brown to dark brown, nearly smooth; nodes annulate, the upper surface being marked by large cup-shaped scars, the lower surface with numerous root-scars or remains of roots; fracture short, the fractured surface mealy or horny, whitish to pale brown, with a circle of small wood-bundles, and a large pith; odor slight, more pronounced and characteristic in the powder; taste sweetish and disagreeably bitter and acrid.	(Official description.)
CANTHARIS.	(Official Latin name.)
CANTHARIDES.	(Official English name.)
The beetle, *Cantharis vesicatoria*, Linné, thoroughly dried at a temperature not exceeding 40° C. (104° F.).	(Official definition.)
From 18 to 25 Mm. long, about 6 Mm. broad; flattish-cylindrical, with filiform antennæ; black in the upper part, with two long wing-sheaths, and ample membranous, transparent, brownish wings; elsewhere of a shining coppery-green color; odor strong and disagreeable; taste slight, afterward acrid. The powder is greenish brown, with shining green particles, and contains few or no hairs; ash not more than 8 per cent.	(Official description.)

The **official Latin name**, which very properly is given in the Latin language, owing to its security against change, is intended to be at once simple and distinctive, and must be accepted as representing the drug or preparation more particularly defined in the other subdivisions. In some instances the names by which drugs have been long known have been retained without any special reference to the source, thus *Galla*, *Buchu*, *Cusso*, *Opium*, *Mastiche*, *Senna*, *Kino*, *Sabal*, etc.; but in the majority of cases the generic or specific name of the plant or animal yielding the drug has been adopted as the official name, thus, *Aconitum*, *Camphora*, *Arnica*, *Ipecacuanha*, *Coccus*, *Hyoscyamus*, *Moschus*, *Rheum*, *Senega*, etc. In order to avoid confusion a few of the former generic or specific names of plants have been retained as the official names of drugs now known to be derived from a different source, as in the case of *Asafœtida* from *Ferula fœtida*, *Cambogia* from *Garcinia Hanburii*, *Pareira* from *Chondrodendron tomentosum*, etc.

When different species of the same genus furnish different drugs it becomes necessary either to employ the full botanical name of the plants to distinguish the official varieties, as *Viburnum Opulus* and

Viburnum prunifolium, or to select the generic name only for one of the drugs and a qualified name for others. Thus, the Pharmacopœia has chosen the generic name *Cinchona* to designate the barks of *Cinchona Ledgeriana*, *Cinchona Calisaya*, *Cinchona officinalis*, and of hybrids of these with other species, which are usually designated as Calisaya or Yellow Bark, and the name *Cinchona rubra* as the official title of the bark of *Cinchona succirubra* and its hybrids, commonly termed Red Bark.

Whenever different parts of the same plant are officially recognized as distinct drugs, the name of the particular part must be added to the generic or specific name of the plant, thus *Belladonnæ Folia* and *Belladonnæ Radix*, *Colchici Cormus* and *Colchici Semen*, etc.; to this rule the Pharmacopœia makes an exception in the case of Sassafras bark and pith, both derived from *Sassafras variifolium*—the bark is officially known by the generic name of the plant, while the pith is designated as *Sassafras Medulla*.

In the official names of compound preparations the principal active constituents are as a rule specified, as *Liquor Ferri et Ammonii Acetatis*, *Tinctura Aloes et Myrrhæ*, *Trochisci Glycyrrhizæ et Opii*, *Pilulæ Aloes et Ferri*, *Mistura Rhei et Sodæ;* but usage has sanctioned a modification of this rule when there are many ingredients, by naming one of them with the addition of an adjective, such as *compositus*, *a*, *um* (compound), *aromaticus*, *a*, *um* (aromatic), etc., thus making a simple comprehensive title, as *Spiritus Ammoniæ Aromaticus*, *Tinctura Cinchonæ Composita*, *Pilulæ Catharticæ Vegetabiles*, *Pulvis Morphinæ Compositus*, *Syrupus Hypophosphitum Compositus*, etc.

In the case of chemical compounds where similar combinations of the same elements, or several varieties of the same compound, have received recognition, it is absolutely necessary that the official name include some qualifying term by means of which the character of the substance may at once be recognized, thus *Hydrargyri Chloridum—Corrosivum* and *Mite*, *Hydrargyri Iodidum—Flavum* and *Rubrum*, *Ferri Sulphas—Exsiccatus* and *Granulatus*, etc.

The Latin official names are generally used in the singular number, even though the idea of plurality may be essentially connected with the drug, as in the case of Caryophyllus, Galla, Amygdala, etc.; this is in accordance with the precedent set by the Roman medical writers. Whenever a part of the plant also appears in the official name the following rule prevails: *Semen* (seed), *Cortex* (bark), and *Radix* (root) are always used in the singular, while *Folia* (leaves) and *Flores* (flowers) are invariably used in the plural.

The **official English name** need not necessarily be a literal translation of the official Latin name; in fact, it seems very desirable that a drug should have two distinct names officially recognized, the one confined to the official Latin title, admirably adapted to abbreviation and use in prescriptions, while the other may be employed in the ordinary course of conversation, and is intended for use in commercial transactions and the daily routine of business, as *Blue Ointment* for *Unguentum Hydrargyri Dilutum*, *Brandy* for *Spiritus Vini Gallici*, *Cascara Sagrada* for *Rhamnus Purshiana*, *Red Rose* for *Rosa Gallica*, *Wild Cherry* for *Prunus Virginiana*, etc. Occasionally the English name is used in the plural, while the Latin name is always used in the singular number, as *Cantharides* for *Cantharis*, *Cloves* for *Caryophyllus*. In the case of chemical compounds the official English name often indicates with greater precision the true composition, as *Solution of Mercuric Nitrate* for *Liquor Hydrargyri Nitratis*, *Ferrous Sulphate* for *Ferri Sulphas*, *Ferric Citrate* for *Ferri Citras*, etc.

Prior to the eighth decennial revision of the Pharmacopœia it was customary, in a number of instances, to follow the official English name by a synonym, enclosed in brackets. Since, as a rule, the origin of such synonyms is unscientific and not in strict accord with systematic nomenclature, they have been taken from the body of the book and placed in the Index of the Pharmacopœia for reference. These synonyms are often used for commercial purposes, among the more prominent being *Calomel* for *Mild Mercurous Chloride*, *Glauber Salt* for *Sodium Sulphate*, *Epsom Salt* for *Magnesium Sulphate*, *Black Draught* for *Compound Infusion of Senna*, *Red Precipitate* for *Red Mercuric Oxide*, *Salol* for *Phenyl Salicylate*, *Citrine Ointment* for *Ointment of Mercuric Nitrate*, *Basham's Mixture* for *Solution of Iron and Ammonium Acetate*, *Griffith's Mixture* for *Compound Iron Mixture*, *Basilicon Ointment* for *Rosin Cerate*, *Witch-hazel* for *Hamamelis*, *White Precipitate* for *Ammoniated Mercury*, *German Chamomile* for *Matricaria*, *Roman Chamomile* for *Anthemis*, *Monsel's Solution* for *Solution of Ferric Subsulphate*, *Labarraque's Solution* for *Solution of Chlorinated Soda*, *Carbolic Acid* for *Phenol*, *Tully's Powder* for *Compound Powder of Morphine*, *Lady Webster Pills* for *Pills of Aloes and Mastic*, *Blaud's Pills*, *Ferruginous Pills*, or *Chalybeate Pills* for *Pills of Ferrous Carbonate*, etc.

The **official definition** determines the source and character of the drug or chemical as recognized by the Pharmacopœia. In the case of vegetable drugs the botanical name of the plant yielding the drug is composed of two parts, the generic name and the specific name, always written in the same order of sequence; the first or generic name is invariably begun with a capital letter, and is usually employed as the official Latin name of the drug, while the specific name is only begun with a capital letter when derived from a generic name, as in *Acorus Calamus* and *Cytisus Scoparius*, or from a proper name, as in *Garcinia Hanburii*, or when it is indeclinable, as in *Theobroma Cacao*. The necessity for using the full botanical name of the plant to indicate the source of the official drug is clearly shown in the case of the genus *Lobelia*, of which the Pharmacopœia recognizes only the species *inflata*, although two others, *syphilitica* and *cardinalis*, are also well known; of the genus *Grindelia*, two species (*robusta* and *squarrosa*) are recognized as furnishing the official drug.

Accompanying the botanical name of the plant is the name of the author, printed in Roman type; and following it, enclosed in parentheses, the family to which the plant belongs—thus, *Veronica virginica*, Linné (Fam. *Scrophulariaceæ*).

In the case of official chemicals it becomes necessary to establish the identity of the compound by expressing its exact composition by means of symbolic formulas; thus in the case of sodium phosphate the formula $Na_2HPO_4 + 12H_2O$ specifies clearly the kind officially recognized by that name; other varieties of sodium phosphate, such as $Na_2HPO_4 + 6H_2O$, Na_2HPO_4, or even NaH_2PO_4, or Na_3PO_4, can therefore not be used in prescriptions or official preparations. The official definition of alumen, alum, is $AlK(SO_4)_2 + 12H_2O$, showing that the pharmacopœial alum is potassium alum, or, more strictly speaking, potassium and aluminum sulphate; since commercial alum, as a rule, is ammonium alum, the official definition is important, and necessary to establish the chemical character of the compound to be used as alum in prescriptions and official preparations. The Pharmacopœia recognizes as magnesium carbonate a compound for which the symbolic formula $4MgCO_3.Mg(OH)_2 + 5H_2O$ is given, which shows it to be not true magnesium carbonate, but a substance containing four molecules of magnesium carbonate, one molecule of magnesium hydroxide, and five molecules of water. The official definition for pure morphine, $C_{17}H_{19}NO_3 + H_2O$, recognizes a compound containing one molecule (in this case 5.94 per cent.) of water, and for pure quinine, $C_{20}H_{24}N_2O_2 + 3H_2O$, a compound containing three molecules (in this case 14.28 per cent.) of water. Whenever water is expressed in a symbolic formula, as in the five cases above mentioned, it forms an integral part of that formula, and is shown to be an essential constituent of the official compound; in the majority of cases the presence of such water lends to the compound its power to assume the crystalline form, and is then known as water of crystallization, but when not so required it is known as water of hydration, as in the case of the official magnesium carbonate. Every symbolic formula is followed by a number which expresses the molecular weight of the compound—that is, the sum of the weights of the atoms of component elements; thus in the case of the official bismuth citrate, $BiC_6H_5O_7 = 394.52$, the molecular weight 394.52 is equal to the sum of the weights of all the atoms represented in the compounds, namely, 1 atom of bismuth $= 206.9$, 6 atoms of carbon $= (11.91 \times 6)71.46$, 5 atoms of hydrogen $= (1 \times 5)5$, and 7 atoms of oxygen $= (15.88 \times 7)111.16$, or $206.9 + 71.46 + 5 + 111.16 = 394.52$; official sodium carbonate is given as $Na_2CO_3 + H_2O = 123.19$, in which case the weight of all the atoms of the crystalline compound, including the water, is accounted for in the molecular weight, 123.19, as follows: 2 atoms of sodium $= 22.88 \times 2 = 45.76$, 1 atom of carbon $= 11.91$, 3 atoms of oxygen $= 15.88 \times 3 = 47.64$, twice 1, or 2 atoms of hydrogen $= 1 \times 2 = 2$, and 1 additional atom of oxygen $= 15.88$, or $45.76 + 11.91 + 47.64 + 2 + 15.88 = 123.19$.

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The number following simple elements expresses only the weight of a single atom, as bromine, $Br = 79.36$, sulphur, $S = 31.83$, etc. Atomic and molecular weights are of value in the proper construction of equations for the purpose of demonstrating chemical reactions.

In the case of a majority of the chemical compounds a statement has been added to the official definition, showing the percentage of purity demanded by the Pharmacopœia. This purity rubric, as it is termed, immediately precedes the official description, see page 19.

The Official Description.—While the official definition is a brief but exact statement of the nature and source of drugs and of the composition of chemicals, the official description amplifies the definition by adding the physical characteristics of drugs, such as shape, size, odor, and taste, together with a statement of possible impurities and adulterations, and means for their detection. For chemicals, are added a clear account of their physical properties, their behavior toward different solvents, and such tests as shall enable the pharmacist to detect impurities and establish the fulfilment of pharmacopœial requirements. The official description is always printed in small type, and forms a most valuable and important part of the Pharmacopœia.

DISPENSATORIES.

A dispensatory is a commentary on the Pharmacopœia, and, as such, has become indispensable to both physicians and pharmacists. While the text of the Pharmacopœia is confined to the definition and description of drugs and chemicals as well as to the official tests and requirements and accepted formulas for numerous preparations, much valuable additional information is given in the dispensatories, such as historical data, action, and uses, as well as doses of medicines, together with comments on and explanations of pharmaceutical and chemical processes. Besides the official drugs and chemicals, a large number of unofficial remedies and formulas are also treated in detail. Three dispensatories are published in this country: the *United States Dispensatory*, established in 1833, by Wood and Bache, which has reached its eighteenth edition, and is now edited by Wood, Remington, and Sadtler; the *American Dispensatory*, first edited by John King, M.D., in 1854, of which the eighteenth edition, entirely rewritten by Lloyd and Felter, was issued in two volumes in 1898 and 1900; and the *National Dispensatory*, established in 1879 by Stillé and Maisch, of which five editions were published, and which, after the death of the original authors, has now been superseded by the *National Standard Dispensatory*, edited by Hare, Caspari, and Rusby.

CHAPTER II.

WEIGHTS AND MEASURES.

Metrology (from the Greek *μέτρον*, measure, and *λόγος*, a discourse) is a study of the art and science of measurements as applied to extension, volume, and weight of matter. Measure of extension may be either of length or of surface, while measure of volume or bulk applies to the cubic contents. Measure of weight is the determination of the gravitating force of bodies—that is, of their attraction by the earth toward its center, such attraction bearing a direct relation to the quantity of matter contained in a body; hence weight is pressure exerted by a body upon a horizontal plane supporting it; and the operation of weighing may be defined as the process of determining the number of standard masses (grammes, grains, ounces, or pounds, as the case may be) which are attracted by the earth with as much force as is the body that is being weighed. True weight can be obtained only *in vacuo*, where the exact measurements of the force of gravitation cannot be interfered with by atmospheric pressure; all measurements of weight in any medium, such as air or water, must therefore give low results. Ordinary operations of weighing, being conducted in air, give apparent weight of the substance only.

Weighing and measuring being operations of daily occurrence in pharmacy which require care and exactness, a knowledge of the standards of weights and measures in use in this country and elsewhere is absolutely necessary. With more or less modification the standards at present in use in pharmacy in the United States and Great Britain are the same as those formerly employed by the Romans, and which in all probability were derived by them from the more ancient Greek nation. Three different systems of weights are at present employed by all English-speaking nations, namely, avoirdupois weight, apothecaries' weight, and metric weight.

Avoirdupois weight, as its name would seem to indicate, is probably of French origin (*avoir du poids*, to have weight), and was no doubt introduced into Great Britain during the reign of the Norman dynasty; it first appeared in the English statute-books in 1335. Avoirdupois weight is employed in the sale of all commodities except precious metals and precious stones; hence drugs are always bought and sold by pharmacists by this system. In Great Britain avoirdupois weight is also employed in the formulas of the British

Pharmacopœia, and is now known there under the name of Imperial weight. In 1824 the value of an avoirdupois pound was defined by law in England to be $\frac{7000}{5760}$ of the old standard troy pound. The divisions of avoirdupois weight are the pound, ounce, drachm, and grain, which are symbolized by the following characters: lb., oz., drm., gr.; each pound contains 16 ounces and each ounce 16 drachms or 437½ grains. The term drachm is rarely employed, quantities less than an ounce being usually designated by common fractions, such as $\frac{1}{16}$ oz., $\frac{1}{8}$ oz., $\frac{1}{4}$ oz., or in grains. The avoirdupois pound containing 7000 grains (437½ × 16) is the only pound used in the United States and Great Britain except at the mints; the standard pound is the equivalent in weight of 27.7015 cubic inches of distilled water at 62° Fahrenheit and normal barometric pressure.

Apothecaries' weight was probably derived from troy weight, which latter was introduced into Great Britain, by merchants from Lombardy, toward the close of the thirteenth century; it is employed altogether in the writing and compounding of physicians' prescriptions, and is divided into grains, scruples, drachms, and ounces, of which 20 grains are equal to 1 scruple, 3 scruples are equal to 1 drachm, and 8 drachms are equal to 1 ounce. The apothecaries' ounce is of the same value as the now obsolete English troy ounce. The following symbols are employed to designate the divisions of apothecaries' weight, and always precede the number indicating the quantity intended, which is expressed in Roman numerals: thus, gr. j, for one grain, ℈ij, for two scruples, ʒiij, for three drachms, ℥iv, for four ounces. As far back as 1266, during the reign of Henry III., a statute was enacted in England which provided that an English silver penny, called a sterling, round and without clipping, should equal in weight 32 wheat-grains, well dried and taken from the centre of the ear, and that of such pence 20 should make 1 ounce, and 12 ounces 1 pound. About 1497, in the time of Henry VII., the weight of the silver penny, however, was changed to the equivalent of 24 wheat-grains. These statutes clearly indicate the origin of the pennyweight and the troy system, from which the apothecaries' weight, still in use at the present day, was subsequently derived. The choice of wheat-grains from *the centre of the ear* arose from a desire for uniformity in size and weight, as did likewise the directions to employ the grain *well dried*. The adoption of troy weight by physicians and pharmacists dates back to 1618, when the first London Pharmacopœia was compiled. In 1826 Imperial measures and standards were legalized in England, and in 1827 exact copies of these standards were furnished the minister of the United States Government at London, namely, the standard yard, a bronze bar of 36 inches length, a brass troy-pound weight of 5760 grains, and a brass avoirdupois-pound weight of 7000 grains; copies of these standards were supplied to the different States in 1836 by Act of Congress. The length of the standard yard is determined by comparison with a pendulum beating seconds of mean time, in a vacuum, at the temperature of 62° Fahrenheit, at the level of the sea, in the latitude of London; the length of such a pendulum was found to be 39.13929 inches.

From what has been said above it is clear that every troy or apothecaries' ounce is heavier than the avoirdupois ounce by 42½ grains; hence to find the corresponding value in avoirdupois ounces of any given number of troy or apothecaries' ounces, add to the latter $\frac{42\frac{1}{2}}{437\frac{1}{2}} = \frac{85}{875}$ or $\left(\frac{17}{175}\right)$ of that number; thus ℥xxiv = 24 avoirdupois ounces plus $\frac{17}{175}$ of 24, which is 24 + 2.33, or 26.33 ounces; or multiply the number of troy ounces by 480 and divide the product by 437.5, the quotient representing the corresponding avoirdupois weight in ounces. If, on the other hand, avoirdupois weight is to be converted into apothecaries' or troy weight, subtract from the number of ounces given $\frac{42\frac{1}{2}}{480} = \left(\frac{85}{960} \text{ or } \frac{17}{192}\right)$ of the number; thus 26.33 ounces $= 26.33 - \frac{17}{192}$ of 26.33, which is equal to 26.33 — 2.33, or 24 apothecaries' or troy ounces; or multiply the number of avoirdupois ounces by 437.5 and divide the product by 480, the quotient representing the corresponding apothecaries' or troy weight in ounces.

While apothecaries' weight is employed in compounding prescriptions both in this country and Great Britain, it is not used in either the United States or the British Pharmacopœia, and will no doubt be entirely abolished in the course of time, when a uniform international system of weights shall have been adopted by the medical and pharmaceutical professions of both countries. The grain is the connecting link between avoirdupois, troy, apothecaries', and Imperial weight, being the same in all.

The fluid measure used by pharmacists of the United States is derived from the old wine measure of England (now extinct), which allowed to each wine gallon the volume of 231 cubic inches, or 58340.011 grains of distilled water at 15° C. (59° F.); the Imperial gallon of Great Britain contains 277.273 cubic inches, or 70,000 grains of distilled water at 62° Fahr. In both cases the gallon is divided into 8 pints; but the pint of wine measure contains 16 fluidounces, while the Imperial pint contains 20 fluidounces. The United States fluid measure has the following units: the minim, the fluidrachm, and the fluidounce, which are represented by the following signs: ♏, fʒ, f℥; in addition, the pint and gallon are sometimes employed in commercial transactions, being designated by the abbreviations *O*, from *Octarius*, for pint, and *Cong.*, from *Congius*, for gallon. The units of Imperial fluid measure bear the same names as those employed for United States fluid measure, but differ from them in value; thus, while the Imperial minim of water weighs 0.91 (0.9114583) grain, the United States minim of water weighs 0.95 (0.9493) grain, and, since both fluidounces contain 480 minims, the Imperial fluidounce of water weighs 437.5 grains, but the United States fluidounce 455.70 grains, at 15.6° C. (60° F.). Each fluidounce is divided into 8 fluidrachms and each fluidrachm into 60 minims.

It must not be overlooked that many liquids, although dispensed and sold by the apothecary by fluid measure, are purchased from the manufacturer by weight, and whenever the specific gravity of the liquid differs materially from that of water there must be also a marked difference in the relative volume; thus glycerin, syrups, chloroform, ethers, acids, essential oils, and many chemical solutions are always purchased by weight. The following list shows the number of fluidounces in one pound of the respective liquids, of pharmacopœial quality:

One pound of	Sulphuric Acid measures about			8⅓	fluidounces.
" "	Monsel's Solution measures about			10	"
" "	Chloroform	"	"	10⅓	"
" "	Syrup	"	"	11¾	"
" "	Glycerin	"	"	12¼	"
" "	Goulard's Extract	"	"	12⅞	"
" "	Ammonia Water	"	"	16	"
" "	Stronger Ammonia Water measures about			17	"
" "	Spirit of Nitrous Ether	"	"	18¼	"
" "	Essential Oil measures from			13 to 18	"
" "	Ether measures about			21⅙	"

The **metric** or **decimal** system of weights and measures, which is the only official system of the present United States Pharmacopœia, is supposed to have originated in the fertile mind of the French statesman, Prince de Talleyrand, toward the close of the eighteenth century, and was enforced in France by law in December, 1799. It has already become the legal standard in all civilized countries except the United States and Great Britain, and is destined to become the universal standard for commercial transactions, as it is already for strictly scientific work, the world over.

The use of metric weights and measures was legalized in the United States and Great Britain in 1866, but neither country has as yet officially adopted them, although the prospects for such desirable action are brightening. In 1878 the use of the metric system was made obligatory in the purchase of medical supplies for the United States Marine-Hospital Service. For some years past, efforts have been made annually by the American Pharmaceutical Association to induce Congress to pass laws looking to the introduction of the metric system of weights and measures in place of those now in use, but thus far without success. Since the introduction of a new system of weights and measures must, no doubt, for a time create some confusion, a careful study of the same is required of pharmacists and physicians. The principles upon which the metric system was founded are as follows: The reduction of all weights and measures to one uniform standard of linear measure; the use of an aliquot part of the earth's circumference as such standard; the application of the unit of linear measure to matter in its three modes of extension—length, breadth, and thickness—as a standard of all measures of length, surface, and solidity; the cubic contents of linear measure in distilled water at the temperature of its greatest density to furnish at once the standard measure of weight and of capacity; everything susceptible of being weighed or measured to have only one measure of weight, one measure of length, and one measure of capacity, with their multiples and subdivisions exclusively in decimal proportions; and every weight and every measure to be designated by an appropriate significant characteristic name applied exclusively to itself.

As a basis, the authors of the metric system adopted a quadrant (one-fourth) of the earth's circumference, and dividing this into ten million parts they obtained a certain measure of length, which they named METER (French *mètre*) and adopted as a standard for all units of measurements; this meter, which was made the unit of linear measure, is equal to 39.3704 inches. One-tenth part of the meter, applied to cubic measurement, was made the unit of measure of capacity and called a LITER (French *litre*); it is equal to 33.8149 U.S. fluidounces or 2.1135 wine pints. The one-thousandth part of the liter (which is equal to the cube of one-hundredth part of the meter) was chosen to furnish the unit of weight; the weight of such a volume of distilled water at its greatest density, 4° C. (39.2° F.), was called a GRAMME, and is equal to 15.43235639 grains. The multiples of these units are denoted by prefixes of the Greek numerals, *deka* 10, *hecto* 100, *kilo* 1000, *myria* 10,000; while prefixes of the Latin numerals denote the subdivisions, thus *deci*, one-tenth; *centi*, one-hundredth, and *milli*, one-thousandth. Two other units of the metric system, the *are* (the square of ten meters) and the *stere* (a cubic meter), are not of pharmaceutical interest. Although the liter is the unit of measures of capacity, the subdivisions of this unit are almost invariably spoken of as so many cubic centimeters, since each liter is equal to 1000 cubic centimeters; thus the expressions 10, 50, 100, 250, 750 cubic centimeters, etc., are preferred to 1 centiliter, 5 centiliters, 1 deciliter, one-fourth of a liter, and three-fourths of a liter. In like manner the specific names of the fourth multiple of the units are rarely employed, it being customary to designate all above the third multiple as so many of that multiple; thus 10 kilometers instead of 1 myriameter, 15,000 liters instead of 1½ myrialiter, and 20 kilogrammes instead of 2 myriagrammes, etc. When writing the names of metric measures and weights, abbreviations are usually employed in place of the full names, as will be seen from the following tables, which also give the corresponding values in customary weights and measures:

Measures of Length.

1 Myriameter,	Mm.	= 10000.0	M	= 6.2137 +	miles.
1 Kilometer,	Km.	= 1000.0	"	= 4.9710 +	furlongs.
1 Hectometer,	Hm.	= 100.0	"	= 19.8840 +	rods.
1 Dekameter,	Dm.	= 10.0	"	= 32.8086 +	feet.
1 Meter,	M.	= 1.0	"	= 39.3704	inches.
1 Decimeter,	dm.	= 0.1	"	= 3.93704	"
1 Centimeter,	cm.	= 0.01	"	= 0.393704	inch.
1 Millimeter,	mm.	= 0.001	"	= 0.0393704	"

Measures of Capacity.

1 Myrialiter,	Ml.	= 10000.0	L.	= 2641.7890 +	gallons.
1 Kiloliter,	Kl.	= 1000.0	"	= 264.1789 +	"
1 Hectoliter,	Hl.	= 100.0	"	= 26.4178 +	"
1 Dekaliter,	Dl.	= 10.0	"	= 2.6417 +	"
1 Liter,	L.	= 1.0	"	= 33.8149 +	fluidounces.
1 Deciliter,	dl.	= 0.1	"	= 3.38149 +	"
1 Centiliter,	cl.	= 0.01	"	= 0.338149 +	fluidounce.
1 Milliliter,	ml.	= 0.001	"	= 0.0338149 +	"
1 Cubic centimeter,	ccm.	= 0.001	"	= 0.0338149 +	"

Measures of Weight.

1 Myriagramme,	Mg.	= 10000.0	Gm.	= 22.0461 +	pounds.
1 Kilogramme,	Kg.	= 1000.0	"	= 2.2046 +	"
1 Hectogramme,	Hg.	= 100.0	"	= 3.5273 +	av. ozs.
1 Dekagramme,	Dg.	= 10.0	"	= 154.3235639	grains.
1 Gramme,	Gm.	= 1.0	"	= 15.43235639	"
1 Decigramme,	dg.	= 0.1	"	= 1.543235639	"
1 Centigramme,	cg.	= 0.01	"	= 0.1543235639	grain.
1 Milligramme,	mg.	= 0.001	"	= 0.01543235639	"

The U. S. Pharmacopœia deviates from these abbreviations in three instances, using *Mm.* in place of *mm.* for millimeter, *Cm.* in place of *cm.* for centimeter, and *Cc.* in place of *ccm.* for cubic centimeter. The numerical expression of all weights and measures should always be accompanied by the abbreviation used for the unit, and whenever subdivisions are not given a cipher should follow the decimal point, so as to indicate more clearly the intention of the writer; thus, 25.0 Gm. and 350.0 Cc., leave no doubt whatever as to the quantities desired, whereas 25 Gm. and 350 Cc. might have been carelessly written for 2.5 Gm. and 35.0 Cc. Since the value of the numerical expression depends entirely upon the correct placing of the decimal point, due care must be observed lest the misplacement thereof increase or decrease the intended value tenfold. When reading metric weights and measures the multiples of the units should be read as so many units, but the subdivisions are preferably named as so many of the lowest division possible; for instance, 25.050 Gm. should be read 25 grammes and 50 milligrammes instead of 25 and $\frac{5}{100}$ grammes; 0.125 Gm., 125 milligrammes instead of $12\frac{1}{2}$ centigrammes or 1 decigramme 2 centigrammes and 5 milligrammes; 0.020 M. should be read as 2 centimeters or 20 millimeters, but never as $\frac{2}{100}$ or $\frac{20}{1000}$ of a meter; 1.425 L. should be read as 1425 cubic centimeters instead of $1\frac{425}{1000}$ liter or 1 liter and 425 cubic centimeters.

The corresponding values, in customary weights and measures, of a few metric weights and measures should be firmly fixed in the mind for convenient use while reading or studying ; as,

1 Mm. (millimeter) = $\frac{1}{25}$ of an inch.
1 Cm. (centimeter) = ⅖ of an inch.
1 inch = 25 millimeters or 2½ centimeters.
1 Cc. (cubic centimeter) = 16.23 minims or 0.27 fluidrachm or 0.0338 fluidounce.
1 fluidounce = 29.57 + (practically 30) cubic centimeters at 4° C. (39.2° F.).
1 Gm. (gramme) = 15.4324 grains.
1 grain = 0.06479 + gramme or 64.79 milligrammes.
1 Mg. (milligramme) = 0.01543 grain (practically $\frac{1}{65}$ grain).
1 L. (liter) = 33.815 (nearly 34) fluidounces or 2⅛ pints.
1 ounce avoirdupois = 28.35 grammes.
1 pound avoirdupois = 453.6 grammes.

In larger commercial transactions the kilogramme is the metric weight generally employed, being frequently abbreviated "kilo"; it is equivalent to 2⅕ avoirdupois pounds + 34 grains.

The following simple rules will enable anyone readily to convert metric weights and measures into those customary in this country, the results being practically correct.

For linear measure: Divide the number of millimeters by 25, 300, or 900; the quotient will be the answer in inches, feet, or yards, respectively.

For measures of capacity: Divide the number of cubic centimeters by 0.06161, 3.697, or 29.57; the quotient will be the answer in U. S. minims, fluidrachms, or fluidounces, respectively.

For weight: Divide the number of grammes by 0.06479, 3.8874, or 31.103; the quotient will be the answer in grains, drachms, or apothecaries' ounces, respectively. If the number of grammes be divided by 28.35 or 453.6, the quotient will be the answer in ounces or pounds, avoirdupois weight, respectively.

In the actual operations of weighing and measuring, however, it will be found more desirable to be provided with a set of accurate metric weights and measures; for then even the slight errors arising from the translation of one system into another can be avoided.

COMPARATIVE TABLE OF METRIC WITH AVOIRDUPOIS AND APOTHECARIES' WEIGHTS.

Names.	Numerical Expressions.	Equivalents in Grains.	Equivalents in Avoirdupois Weight.			Equivalents in Apothecaries' Weight.		
	Gm.	Gr.	lb.	oz.	gr.	℥	ʒ	gr.
Milligramme	0.001	0.01543	...	...	$\frac{1}{64}$	...	...	$\frac{1}{64}$
Centigramme	0.010	0.15432	...	...	$\frac{1}{6}$	...	...	$\frac{1}{6}$
Decigramme	0.100	1.54323	...	...	1.5	...	...	1.5
Gramme	1.0	15.43235	...	...	15.4	...	...	15.4
Dekagramme	10.0	154.32356	...	¼	45.0	...	2	34.0
Hectogramme	100.0	1543.23563	...	3½	12.0	3	1	43.0
Kilogramme	1000.0	15432.35639	2	3¼	10.47	32	1	12.4
Myriagramme	10000.0	154323.56390	22	½	14.8	321	4	3.5

In writing prescriptions, physicians are in the habit of considering 4 Cc. (actually 3.6969) as equivalent to 1 fluidrachm, and 30 Cc. (actually 29.573) as equivalent to 1 fluidounce.

COMPARATIVE TABLE OF METRIC AND APOTHECARIES' FLUID MEASURE.

Cubic Centimeter.	Minims.	f℥	fʒ	♏
0.06161 –	1.0	...	...	...
0.30805	5.0	...	...	...
0.61610	10.0	...	...	...
1.0	16.23	...	...	...
5.0	81.15	...	1	21.15
10.0	162.30	...	2	42.3
20.0	324.60	...	5	24.6
30.0	486.90	1	0	6.9
40.0	649.20	1	2	49.2
50.0	811.50	1	5	31.5
60.0	973.80	2	0	13.8
70.0	1136.10	2	2	56.1
80.0	1298.40	2	5	38.4
90.0	1460.70	3	0	20.7
100.0	1623.00	3	3	3.0
250.0	4057.50	8	3	37.5
500.0	8115.00	16	7	15.0
1000.0	16230.00	33	6	30.0

Physicians and pharmacists cannot be too careful in the use of metric weights and measures in the writing and reading of prescriptions. In continental Europe, where the metric system has been in use for many years, no signs are used in prescriptions, because all ingredients, whether solid or liquid, are weighed, and it is understood that weight is always intended; whenever, for any reason, measures are wanted, the signs L. (liter) and Ccm. (cubic centimeter) are employed. But in this country, and also in England, where it is still, and likely to remain, customary to weigh solids and to measure fluids in the dispensing of medicines, the official abbreviations given in the U. S. Pharmacopœia should be used invariably, so as to avoid all possible confusion. With water, and the average diluted alcohol tinctures, it would probably not make much difference whether grammes or cubic centimeters were dispensed, but in the case of all liquids having a higher or lower specific gravity than water a marked variation will be observed; thus 20 Gm. of glycerin measure 16 Cc., and 20 Cc. of glycerin weigh 25 Gm.; 60 Gm. of simple syrup measure 45.5 Cc., and 60 Cc. of syrup weigh 79.02 Gm.; 30 Gm. of chloroform measure 20.13 – Cc., and 30 Cc. of chloroform weigh 44.7 Gm.; 4 Gm. of bromoform measure only 1.4 Cc., and 4 Cc. of bromoform weigh 11.32 Gm.; 10 Gm. of ether measure 13.77 – Cc., and 10 Cc. of ether weigh only 7.26 Gm.; 50 Gm. of alcohol measure 60.97 – Cc., and 50 Cc. of alcohol weigh 41 Gm.

It is incumbent upon the medical schools of this country to familiarize their students with the decimal system of weights and measures, as is now done in all colleges of pharmacy; and not until the national medical and pharmaceutical associations shall have agreed upon some rule or guide for the two professions in the specification of metric weights and measures in prescriptions will the pharmacist be relieved of annoyance and censure caused by improper interpretation of quantities.

In the absence of specified fluid measures it is safest to follow the custom of continental Europe and weigh all solids and liquids when dispensing prescriptions written in the metric system.

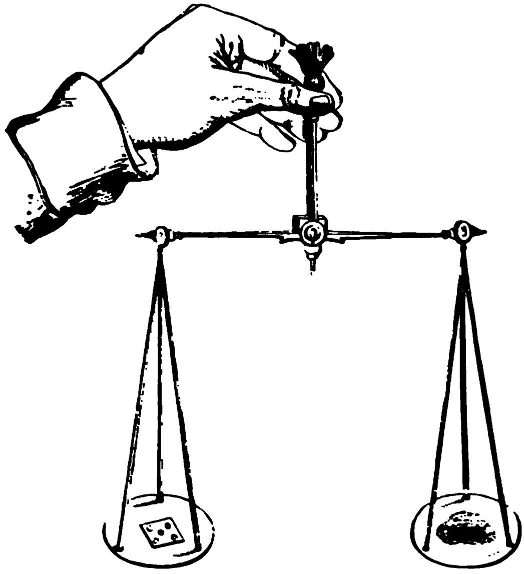
In 1890 the United States Government obtained from the International Bureau of Weights and Measures prototype standards of the Meter and the Kilogramme, made of platinum-iridium; these were placed in the custody of the Office of Standard Weights and Measures at Washington, and from them the commercial weights and measures now in use are derived. The value of the United States prototype standard Meter and Kilogramme is identical with the international standards derived from the Mètre and Kilogramme "des Archives" of France.

The United States yard is defined to be equal to $\frac{360000}{393700}$ of a meter; the pound (avoirdupois) is defined as being equal to $\frac{700000000}{1543235639}$ of a kilogramme; and the liquid gallon is the volume of 3785.434 grammes (58418.1444 grains) of water at the temperature of its maximum density, weighed in vacuo.

The instruments used in weighing and measuring are balances, weights, and graduated vessels, and the necessity for their accuracy and careful preservation cannot be too strongly emphasized.

The **balance,** or, as it is commonly called, "a pair of scales," is no doubt the most useful instrument in the hands of the pharmacist, for upon its proper construction and sensitiveness depend the accuracy of weighing and correct dispensing of medicines. The general construction of an ordinary balance is so well known that a detailed description seems unnecessary; the simple hand scales (see Fig. 1), which were formerly relied upon altogether, have almost completely disappeared in this country; in their stead a more substantial instrument is now used. The single beam principle still prevails, in which a metallic bar is supported at its centre on a knife-edged axis, called the fulcrum, thus producing two arms of equal length. The fulcrum projects from the sides of the beam, and rests on two supports at the top of a stationary column, so constructed that the wear and tear due to constant friction is relieved by a special contrivance for raising the beam above the steel or agate plane when the balance is not in actual use. The knife-edged axis and the support on which it rests are both made of hardened steel and highly polished, in order to reduce friction to a minimum; but since even steel is liable to become rusty, particularly when exposed to moisture or acid vapors, agate edges and planes, which are practically indestructible, are now preferred on all finer balances. The centre of gravity of the beam, which is the point through which the sum of the separate attractions of all the particles of the beam passes and operates as one force, should be located slightly below the edge of the fulcrum; if it were in the edge of the fulcrum, the beam would not come to a horizontal position when the pans are equally loaded, but would remain in any position where it might chance to be placed. If it were above the edge of the fulcrum, the beam would remain horizontal if placed so; but if slightly deflected, it would tend to overturn by the action of the weight of the beam. The nearer the centre of gravity comes to the edge of the fulcrum, the more accurate and sensitive will the balance be; but at the same time the beam will turn more slowly. The scale-pans are suspended in suitable wire frames, also supported by means of knife edges from the ends of the beam; in order to insure perfect equilibrium it is essential that the end knife edges be situated equally distant from the central point of support, and that they lie in the same plane with it, all three edges being parallel to each other. The lighter in weight and the more inflexible the beam, the greater will be the sensitiveness of the balance. Both of these desirable qualities are obtained by the use of aluminum beams, which are also non-corrosive and non-magnetic.

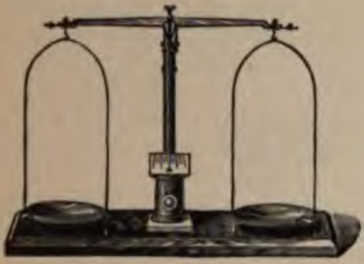
FIG. 1.



Old-style hand balance.

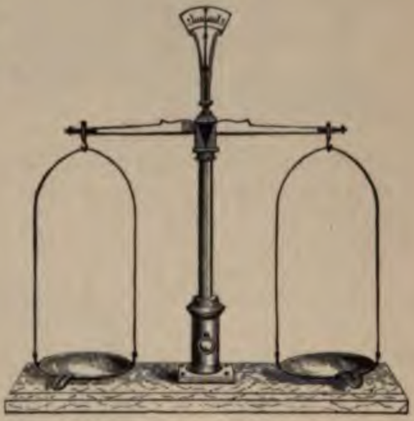
The scale-pans are preferably made of solid nickel or solid silver; but for weighing certain chemical substances likely to attack the metal they should be supplanted by strong glass pans. Each balance is provided with an indicator in the form of a long, thin, flat needle attached to the centre of the beam, and so arranged that when the beam is in perfect stable equilibrium it points directly to the zero mark on a short graduated plate attached to the front base of the upright (see Fig. 2); on some balances the indicator points upward, the graduated scale being placed at a little distance above the beam (see Fig. 3). When the balance is in use, it is far better to rely upon the regular, uniform oscillations of the beam, as shown by the indicator on the scale, than to await the fixed position of the indicator at the zero point. Every balance when purchased should be carefully tested as to its sensitiveness and correct adjustment; this is best done by allowing the beam to oscillate freely supported on its fulcrum, with the pans detached. The oscillations should be regular and the beam finally return to its horizontal position of rest; but it must be borne in mind that an essential requisite for the success of this test is a perfectly level position of the balance. The equilibrium of the beam should also be maintained when the pans are attached, whether empty or lightly or heavily loaded, and when the load is transposed from one pan to the other; these tests prove equality in the length of the arms. Prescription balances, sensitive to $\frac{1}{100}$ grain and intended only for weighing small quantities, whereby their accuracy can be maintained for a very long time, are offered of superior workmanship and provided with spirit level, levelling screws, and other devices to insure correctness in weighing (see Fig. 4). All fine balances should be kept enclosed in a suitable case provided with glass sides and top to protect them against dust, moisture, and corrosive vapors; they should not be scoured at any time, but simply polished with a piece

FIG. 2.



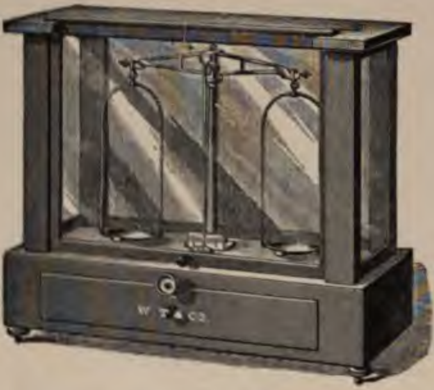
Prescription balance with indicator below the beam.

FIG. 3.



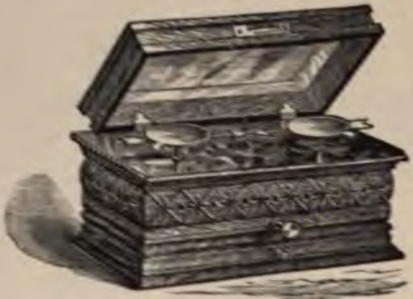
Prescription balance with indicator above the beam.

Fig. 4.



of soft chamois skin or dusted with a soft camel-hair brush; under no circumstances should oil or chalk be used on the knife edges or planes.

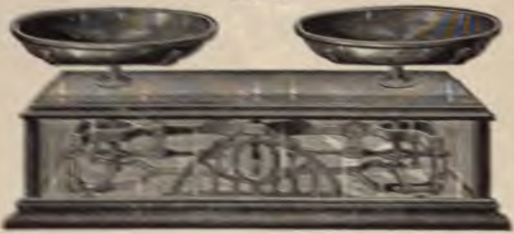
Fig. 5.



Prescription box scales.

Compound lever balances differ from those above described chiefly in having the pans situated above the beam and supported

Fig. 6.

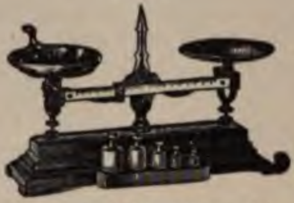


Compound lever balance.

upon rods so constructed as to retain their vertical position during oscillation; they are less sensitive than the single beam prescription balances, and are generally used for coarser weighing. When enclosed in a box they are known as "box scales," and then possess the advantage of having the more delicate parts of the mechanism protected against injury.

Figs. 5 and 6 show prescription and counter box scales constructed on the compound lever principle. Fig. 7 represents a convenient dispensing balance for rough prescription work, and is intended for quantities ranging from 30 grains to 4 ounces; it is sensitive to ½ grain, and is provided with a beam graduated into apothecaries' and metric weight (1 to 120 grains and 0.1 to 8.0 Gm.) and carrying a sliding poise.

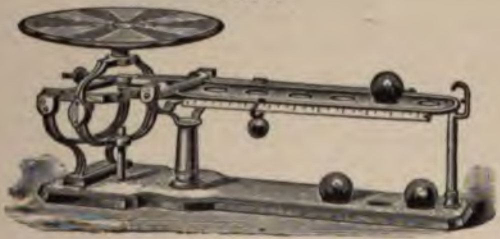
FIG. 7.



Troemner's dispensing scale.

Special balances for weighing liquids, particularly in the laboratory, have been found very convenient on account of their peculiar construction. Fig. 8 repsents Troemner's new solution balance, capable of weighing from 10 grammes to 16 kilogrammes (154 grains to about 36 pounds). The scale is provided with an extra balancing beam, by which an empty bottle or container is quickly balanced by simply sliding the balance weight along until a correct balance is secured. A new system of adjusting weights, known as the ball system, is attached, and is a great improvement over the old method of using separate weights; small weights are adjusted on the graduated beam in front, while the larger weights are represented by different positions of the balls on the central plate.

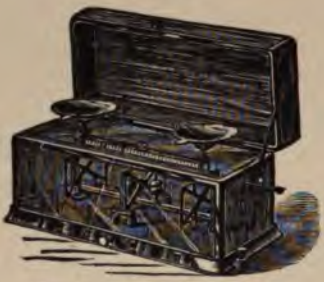
FIG. 8.



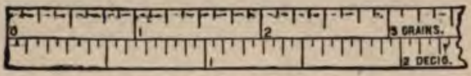
Troemner's new solution balance.

Since 1882 great improvements have been made in what are known as *torsion balances*. The chief differences between torsion and ordinary balances are the entire absence of knife edges and the location of the centre of gravity above the fulcrum or point of rotation. The knife edges have been replaced by thin steel springs stretched tightly between bearings, the centre of the beam being fastened to the centre of the strained spring and at right angles to it; under this condition the beam, by the elasticity or torsion of the spring, will vibrate precisely as the ordinary beam balanced on knife edges. The pans rest upon similar torsion springs at the ends of the beam in the same manner as the central fulcrum of the beam. The inherent torsional resistance to oscillation, due to the tightly stretched wire bands, is overcome by elevating the centre of gravity above the fulcrum, by means of a weight, to such a height that its tendency to reach its lowest position (vertically below the centre of rotation) almost neutralizes the total resistance. If, consequently, the tendency of the high centre of gravity and the resistance of the wire bands are opposed to such an extent as nearly to neutralize each other, the sensitiveness of the balance is established, and the slightest weight placed on the pans will cause the beams to oscillate; on the other hand, the beams will return to their horizontal position by the unneutralized resistance. The foregoing principle has been applied to a variety of balances adapted to ordinary commercial weighing, as well as the more delicate adjustment of fine prescription work and chemical analysis; like ordinary balances, they are provided with graduated beams and poise to be used in place of weights. Fig. 9 represents a torsion prescription balance of fine adjustment, with all the parts enclosed in a glass case and fully exposed to view; it is sensitive to 1 milligramme or $\frac{1}{64}$ of a grain, and up to 500 milligrammes or 8 grains all weights can be adjusted by means of a rider on the graduated beam. Fig. 10 represents a torsion counter balance sensitive to 2 grains, and having a capacity of 20 pounds; it is also provided with a triple graduated beam for avoirdupois, troy, and metric weights.

FIG. 9.



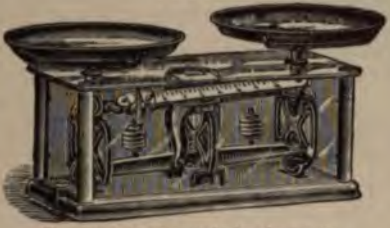
Torsion prescription balance.



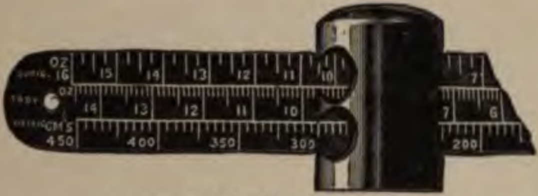
Section of rider beam for same.

Every pharmacist who lays claim to doing even a moderate prescription business should have in his possession at least two balances, one of which may be used for weighing quantities ranging from 30 grains to 2 or 3 ounces, and should be sensitive to at least $\frac{1}{2}$ grain; while the other should be confined to quantities never greater than 2 grammes or 30 grains, and should respond readily to a change in weight amounting to 2 or 3 milligrammes or $\frac{1}{30}$ to $\frac{1}{20}$ grain; besides these a larger balance (usually termed counter scales) is needed for general trade; this should be of such adjustment as to allow accurate weighing thereon of quantities ranging from ½ ounce to 5 or 10 pounds, and should be sensitive to 5 or 10 grains with a full charge.

FIG. 10.



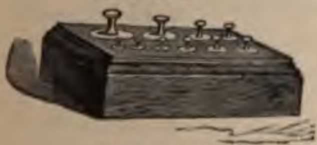
Torsion counter scale in glass case.



Section of triple rider beam for same.

Weights are pieces of metal designed to weigh aliquot parts of the established units; brass or iron is used for the customary commercial weights, while brass or aluminum is chosen for weights employed for dispensing purposes; platinum is also occasionally used for small prescription weights on account of its extreme hardness and resistance to atmospheric influences. Accurate weights are as essential as accurate balances, for one is rendered unreliable without the other. The usual form of smaller commercial weights is in sets known as box or block weights, and ranging from ¼ ounce to 5 pounds (Fig. 11). Troy weights, as a mark of distinction from avoirdupois weights, are usually sold in nests of brass cups (see Fig. 12); they run from ⅛ ounce to 8 or 16 ounces, and for use in dispensing prescriptions the lower denominations, from ¼ grain up to 2 ounces, are frequently put up in boxes or blocks as shown in Fig. 13. The smaller dispensing weights are made either of brass or nickel-silver, after the style shown in Fig. 14, or of aluminum if below the denomination

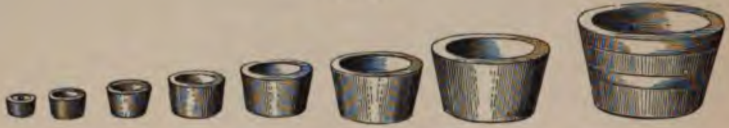
FIG. 11.



Block weights.

of 10 grains (see Figs. 15 and 16); weights less than $\frac{1}{4}$ grain are often indicated by means of a sliding poise on a graduated beam. The relative lightness of aluminum adapts this metal admirably for use in weights of very low denominations, as

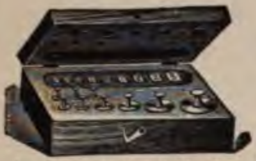
FIG. 12.



Set of apothecaries' cup weights.

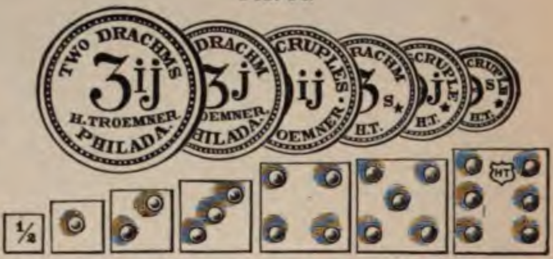
they can be made of larger size and consequently be more conveniently handled than heavier brass weights. Metric weights are made of iron, brass, or aluminum, in the same forms as already described for avoirdupois and apothecaries' weight.

FIG. 13.



Apothecaries' weights (¼ gr. to ʒij) in case.

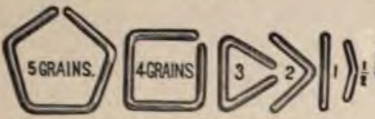
FIG. 14.



Brass or silver-nickel prescription weights.

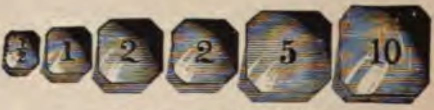
In connection with the operation of weighing, the term *tare* is frequently used to indicate the weight of the empty vessel (dish, box, bottle, or jar) in which the substance (liquid or dry) is to be weighed; *gross weight* is the combined weight of the substance and

FIG. 15.



Aluminum wire weights.

FIG. 16.

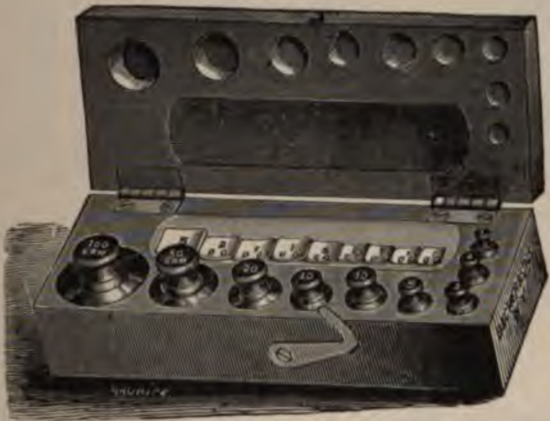


Aluminum grain weights.

the container; *net weight* is the weight of the substance alone, obtained by subtracting from the *gross weight* the *tare* of the container. Instead of finding the exact weight of the container, the latter may be simply *counterpoised* or balanced by small shot or dry coarse sand contained in a suitable cup.

Everyone who has occasion to use fine balances should early accustom himself to certain habits of care and neatness, which will materially preserve the sensitiveness of the instrument. The following rules are recommended: *Never allow the beam to oscillate when the balance is not in use. Immediately after the operation of weighing is completed replace the weights in their proper receptacle and clean the pans with a soft towel. Never weigh deliquescent salts, or active chemicals, such as iodine, on the metal pans, but always on glass or in tared vessels. Always weigh potent or poisonous drugs on stiff glazed paper, using pieces of equal size to counterpoise each other. Never place large weights on the pans, nor remove them, while the beam is in motion,* as the sudden jar produced by the change causes undesirable friction and destroys the sensitiveness of the balance.

FIG. 17.

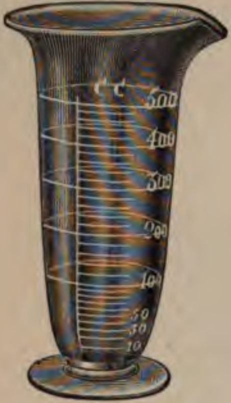


Set of metric prescription weights. (100 grammes to 1 centigramme.)

Measures are vessels used for determining the volume of liquids, and even dry substances; the latter kind do not concern the pharmacist, who is compelled, however, to have on hand a variety of vessels provided with appropriate scales of measurement for liquids. Such vessels are usually made of glass, and are known simply as graduates; they occur of different capacities from 1000 cubic centimeters (1 liter) down to 5 cubic centimeters, and from 64 fluidounces down to 60 minims. The *Phœnix* and *Acme* graduates, manufactured in this country, are guaranteed to be accurate and made strictly according to the American standard of apothecaries' fluid measure; since Imperial measure differs materially from U. S. fluid measure, graduates made in England cannot be used in this country unless they have been adjusted according to the American standard. Very accurate metric graduates are also now made in this country.

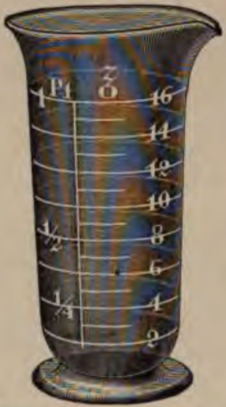
Graduates of different shapes are in use—conical, tumbler-shaped, and cylindrical (see Figs. 18, 19, 20), the last named of which, although the most accurate, are but rarely seen in stores. Cylindrical graduates have a small diameter, which is uniform throughout the height of the vessel; hence errors in measurement due to capillary attraction are in these reduced to a minimum. For $\frac{1}{4}$ and $\frac{1}{2}$ oz. graduates the diameter is about $\frac{1}{2}$ inch; for 1 and 2 oz. sizes it should not exceed $\frac{3}{4}$ inch; while for the 4 oz. size, $1\frac{1}{4}$ inch diameter will be ample. For measuring quantities less than two fluidounces the cone-shaped graduates will be found preferable to the

Fig. 18.



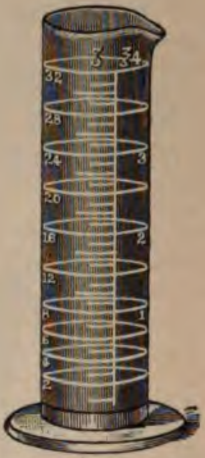
Conical graduate.

Fig. 19.



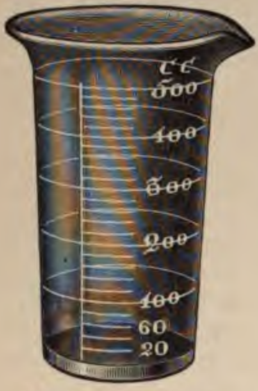
Tumbler-shaped graduate.

Fig. 20.



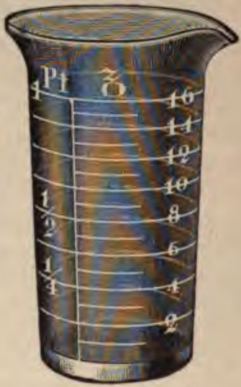
Cylindrical graduate.

Fig. 21.



Metric fluid measure.

Fig. 22.



U. S. fluid measure.

Acme graduates.

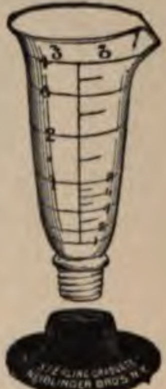
tumbler-shaped, but difficulty is often encountered in cleaning them properly, particularly the smaller sizes. The "Acme" graduates, introduced a few years ago, possess the advantage of being flat on the bottom, without a foot, and hence are less likely to be upset or broken; they are admirably adapted for laboratory work, are cylindrical in form, of about the same diameter as tumbler-shaped graduates, and can be had for both metric and apothecaries' fluid measure (see Figs. 21 and 22).

Duplex graduates, arranged for apothecaries' fluid measure on one side and metric fluid measure on the other, are not to be recommended, on account of the danger of confusion and the greater difficulty of accurate measurement.

Like all glassware, graduates are easily broken, and as the first break usually occurs at the base, either through accident or carelessness, graduates are now made with hard-rubber bases, the glass part being screwed into the base and firmly held. These graduates have been patented, and are sold on the market as "Sterling" graduates; they are claimed by the manufacturers to be strictly accurate (see Fig. 23).

Although minim graduates are extensively employed for measuring volumes of less than $\frac{1}{4}$ fluidounce, it will be found more desirable to use minim pipettes (see Fig. 24) for quantities ranging from 5 to 60 minims; these instruments, first suggested by Dr. E. R. Squibb, are accurately made, and will be found very convenient. For measuring small metric volumes the graduated cubic centimeter pipettes of Dr. Curtman will be found very serviceable (see Fig. 25); they come in different sizes—5, 10, and 25 Cc. capacity—each cubic centimeter being divided into tenths, and are especially adapted for pharmacopœial testing.

Fig. 23.

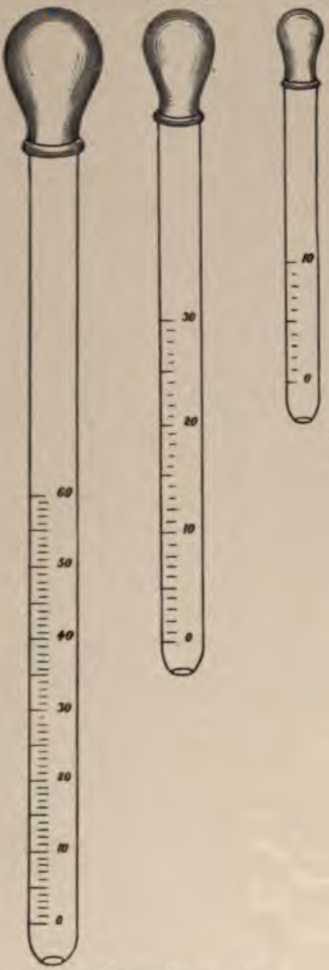


Sterling graduate.

As to the proper manner of holding a graduate while measuring liquids, it may be said that the firmest hold is obtained by grasping the graduate with the left hand in such a manner that the first or index finger encircles the lower part of the vessel, the thumb resting on the base and the second finger forming a support by being placed under the base; this leaves the third and fourth fingers free to remove and hold the stopper of a bottle from which any liquid is to be measured; the mark to which the liquid is to be measured should be on a level with the operator's eye while the graduate is held in an upright position. Owing to capillary attraction, every liquid contained in a graduate will present two concave surfaces, neither of which can be taken as the true level; hence a correct reading of the graduation can only be had by fixing the desired marking of the scale intermediate between the upper and lower edges of the liquid.

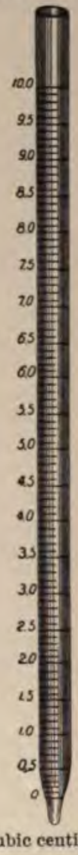
Graduates which have the same scale marked on both sides, or which are encircled by the markings of the scale, admit of more accurate measurements, and do not require that careful attention to levelling the graduate necessary with the plainer varieties.

FIG. 24.



Squibb's minim pipettes.

FIG. 25.



Curtman's cubic centimeter pipette.

Glass graduates are best cleaned by washing with a mop, using soap and water if necessary, rinsing with clear water and allowing the graduate to drain either on a perforated tray or by hanging in a rack; but never should a towel be used to dry the graduate, as it is apt to leave lint adhering to the glass.

Approximate Measurements.—Owing to the varied density of liquids, the number of drops contained in a certain volume must vary greatly with different liquids; moreover, the size of a drop is influenced by the size and shape of the vessel from which the drop is allowed to fall—so that a drop is a very uncertain quantity in the division of doses of medicines. The variability of adhesion to glass exhibited by different liquids, and the rapidity with which liquids flow from the same vessel held at different angles of inclination, are other factors which determine the size of drops, as is shown in the case of chloroform.

Instead of being identical with the minim, drops may vary from one-fifth to one and one-fourth minim.

For the purpose of better illustration, the following short table has been inserted, showing the great variability in size of drops of different liquids:

TABLE SHOWING THE NUMBER OF DROPS TO A FLUIDRACHM.

Liquid.	120 minims Phœnix Graduate.	1 fluidounce Phœnix Graduate.	W. T. & Co's. exact Medicine Dropper.	Pint or Quart Shelf Bottle.
Distilled Water	48	46	128	
Tincture of Aconite	150	150	190	120
" " Belladonna	144	144	174	108
" " Chloride of Iron	150	150	190	120
" " Opium	130	130	154	
" " " Camphorated	136	136	170	
" " Deodorized Opium	90	110	124	80
Glycerin	90	76	90	
Purified Chloroform	234	240	304	160
" " second trial	274	279	360	180
Dilute Hydrocyanic Acid	60	80	75	60 (℥j bottle)

FIG. 26.

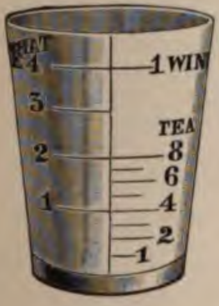


FIG. 27.

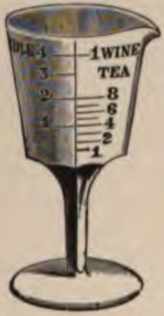
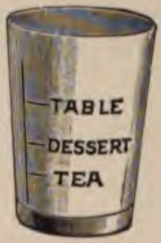


FIG. 28.



Graduated medicine glasses.

For the administration of medicines certain familiar domestic measures are employed, which, although subject to considerable variations, are usually estimated as having the following capacity:

A teaspoonful, equal to one fluidrachm;
A dessertspoonful, equal to two fluidrachms;
A tablespoonful, equal to one-half fluidounce;
A wineglassful, equal to two fluidounces;
A teacupful, equal to four fluidounces; and
A tumblerful, equal to eight fluidounces.

Figs. 26, 27, and 28 represent convenient medicine glasses, well adapted to family use.

These vessels are now obtainable accurately graduated and made to correspond to apothecaries' fluid measure; hence they are preferable to the variable tea-, dessert- and tablespoons generally met with, and should be employed altogether in the sick-room.

The U. S. Pharmacopœia directs that the following values in metric measure should be considered equivalent to the approximate measurements indicated: 4 Cc., 1 teaspoonful; 8 Cc., 1 dessertspoonful; 16 Cc., 1 tablespoonful.

CHAPTER III.

SPECIFIC GRAVITY.

A KNOWLEDGE of the subject of specific gravity is of importance to the pharmacist, as it frequently enables him to detect impurities or to determine the identity and quality of the drugs he handles. Specific gravity does not indicate absolute weight, but merely a relative value, or the relation between the volume and weight of bodies as compared with a standard—the standard for liquids and solids being distilled water, while atmospheric air or hydrogen is used for gaseous bodies; in other words, specific gravity expresses the ratio between the weight of any gaseous, liquid, or solid body and that of an equal volume of the respective standard.

The terms specific gravity and density are frequently used synonymously in pharmacy and chemistry. In physics density is defined to be the mass, or quantity by weight, of a substance in a unit volume, the latter being either a cubic centimeter, as in the metric system, or a cubic foot, as in the English system. In the metric system, where density expresses the number of grammes in a cubic centimeter of a homogeneous substance, density is identical with specific gravity referred to water at 4° C. (39.2° F.), since the gramme is the mass or weight in a cubic centimeter of water at 4° C. (39.2° F.), and thus comparison with the accepted standard is established. This identity, however, vanishes if the specific gravity has been referred to water at a higher temperature; and although the difference between density and specific gravity at such higher temperatures may not be very great, it is sufficient to destroy identity, since 1 cubic centimeter of water above 4° C. weighs less than 1 gramme. In pharmacy and chemistry these slight differences are practically ignored, and hence the terms density and specific gravity are generally used interchangeably, namely, to express the ratio between the mass of a unit volume of water and the mass of a unit volume of the substance being tested. In the English system, where the cubic foot is taken as the unit of volume, density will be expressed by a number 62.4 times as great as the number indicating the specific gravity of a substance at 4° C. (39.2° F.), since a cubic foot of water at 4° C. (39.2° F.) weighs 62.4 pounds, or, in other words, contains 62.4 units of mass. The variations in weight of a cubic foot of water at temperatures above 4° C. (39.2° F.) would have the effect of increasing this ratio (62.4) between density and specific gravity.

As the volume of all bodies varies with temperature, it is essential that the comparison of weights be made at some fixed temperature.

On scientific principles and for the sake of uniformity it is desirable that specific gravity always be referred to water at 4° C. (39.2° F.). In some countries this temperature, at which pure water assumes its greatest density is taken for the comparison of weights, while in the United States Pharmacopœia 25° C. (77° F.) has, with very few exceptions, been fixed as the standard temperature; Great Britain has adopted 15.5° C. (60° F.), and Germany, 15° C. (59° F.). As the comparison of weight of equal volumes of bodies may be made at any temperature desired or convenient, and as the specific gravity will vary accordingly, it is necessary to state the temperature in connection with specific gravity; for instance, to say that a liquid has the specific gravity 1.42 would not indicate at what temperature the liquid had been weighed, nor would it indicate comparison with water at any fixed temperature. To say that a liquid has the specific gravity 1.42 at 15° C. would still leave a doubt as to the temperature at which an equal volume of pure water had been weighed for comparison, for it may have been 4° C., 12° C., or even 25° C., and in either case the specific gravity named would not be correctly stated. To say, however, that a liquid has the specific gravity 1.42 at 15° C. *as compared with water at the same temperature*, leaves no room for doubt as to the true ratio existing between the liquid and water—it therefore expresses true specific gravity. The United States Pharmacopœia (1900) expressly states that all of its specific gravities are to be considered as taken at 25° C. and *compared with water at the same temperature*, whenever no special temperature is mentioned.

Generally it will be found more convenient to weigh substances at ordinary room temperature, 22° C. (71.6° F.) than to cool them to 4° C. or even to 15° C. and keep them cool while weighing, and therefore, assuming that for the majority of pharmacists in the United States a temperature of 25° C. (77° F.) would at all times be more easily attainable and controllable, the Pharmacopœia has adopted this temperature as the official standard for taking specific gravity. This temperature is but very few degrees above the average room temperature, and by using it, the annoying feature of the condensation of atmospheric moisture on the apparatus employed is overcome.

Whenever a body has been weighed at a temperature different from that at which the standard volume of water has been fixed, it is customary to indicate this difference by writing both temperatures in the form of a fraction, the temperature at which the water was weighed being always written as the denominator and the temperature at which the body being tested is weighed as the numerator; thus, the expressions 0.927 at $\frac{15^\circ}{4^\circ}$ C., 1.250 at $\frac{15^\circ}{15^\circ}$ C., and 1.340 at $\frac{25^\circ}{25^\circ}$ C., indicate specific gravities found at 15° C. and 25° C.

as compared with or referred to water at 4° C., 15° C., and 25° C., respectively.

Barometric pressure is not without effect on the relation between the volume and weight of bodies; hence absolute specific gravity, like absolute weight, is obtainable only *in vacuo*; for pharmaceutical purposes this difference is always ignored and the barometric pressure assumed to be normal, 760 Mm. or 30 inches.

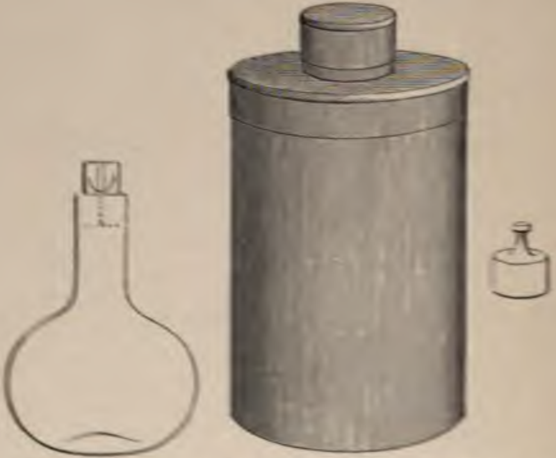
The specific gravity of a solid or liquid is always expressed by a number which shows how much heavier or lighter the weight of a certain volume of water is than the weight of the same volume of that solid or liquid; and the specific gravity of a gaseous body is expressed by a number which shows how much heavier or lighter the weight of a certain volume of atmospheric air (or hydrogen) is than the weight of the same volume of that gaseous body. The specific gravity of water is therefore stated to be 1, and the specific gravity of air (or hydrogen) is likewise stated to be 1. The following simple rule may be given for finding the specific gravity of any liquid or solid substance by calculation: Divide the weight of a given volume of any liquid or solid by the weight of an equal volume of distilled water, both weighings, if possible, having been made at the same temperature. The quotient expresses the specific gravity.

SPECIFIC GRAVITY OF LIQUIDS.

The determination of the specific gravity of liquids is far more frequently required than is that of solids. The different instruments employed for that purpose are specific gravity flasks or pycnometers, loaded glass cylinders, specific gravity beads, and specific gravity spindles or hydrometers. Any small flask, of 25 or 50 Cc. capacity, with a long, narrow neck and made of thin glass, will answer as a specific gravity bottle. Its weight, or tare, is first carefully ascertained and noted; pure water is then poured into the flask until it reaches a short distance up into the neck, when a mark should be made with a file at the upper and lower edge of the meniscus or concave surface; having noted the temperature of the water, the flask and contents are weighed, and from this weight the tare of the flask is deducted, the remainder being the weight of that particular volume of pure water at the given temperature. The tare, temperature, and weight of water are carefully etched on the side of the flask, which is now ready to be used for taking the specific gravity of any liquid, by filling it to the mark in the neck with the liquid to be tested, then weighing and dividing the net weight of the liquid by the weight of the water, the quotient being the specific gravity of the liquid. Suppose the flask weighs 324 grains and holds, up to the mark, 647 grains of water; filled to the mark with sulphuric acid, it weighs 1511.5 grains, which leaves $1511.5 - 324 = 1187.5$ grains as the weight of the acid. Now applying the rule, to divide the weight of a given volume of a liquid by the weight of the same volume of water, the specific gravity is found to be $1187.5 \div 647 = 1.835 +$.

Small glass-stoppered flasks, graduated to hold 100, 250, 500, or 1000 grains of distilled water at 15.6° C. (60° F.), are a more convenient form of pycnometer; they come packed in tin cases, and are accompanied by a metal counterpoise to balance the empty bottle (see Fig. 29). In using these flasks it is necessary to fill them with the liquid to be tested, to a little above the mark in the neck to which the glass stopper reaches when inserted, so that the air and small excess of liquid shall be forced out through the capillary tube drilled through the stopper. The liquid to be tested, having the same temperature as that at which the flask has been adjusted, may be weighed, after wiping the flask dry, when, in the case of the 100- or 1000-grain bottle, the weight at once expresses the specific gravity by simply placing the decimal point correctly, without further calculation; for, as the weight of water (100 or 1000 grains) is to the weight of the same volume of any liquid, so is the specific gravity of water (1.000) to the specific gravity of that liquid. Example: If the 100-grain bottle be found to hold 141.5 grains of a certain acid, the specific gravity of that acid will be 1.415; for $100 : 141.5 :: 1.000 : x$. $x = 1.415$.

Fig. 29.



Glass-stoppered specific gravity bottle with tin case and counterpoise.

Some pycnometers are graduated to hold a definite weight of distilled water at 4° C., while others may be graduated at 12° C., 15° C., 15.5° C., 20° C., 25° C., or some other temperature. Hence, if the weighing of other liquids be made in such pycnometers at a higher or lower temperature than the one at which the flask has been graduated, a suitable correction must be made for the expansion or contraction of water at such temperatures, the change in the glass being usually ignored, since it amounts to but very little. A flask graduated to hold 25 grammes of distilled water at 4° C. will hold but

24.979 grammes at 15° C., and only 24.9285 grammes at 25° C. The cubical expansion of water and other liquids is not uniform for each degree of rise in temperature, and hence a correction by means of an addition or subtraction factor cannot be made. If a pycnometer be graduated at a fixed temperature, and be filled with any other liquid at a higher or lower temperature, the specific gravity of that liquid, as referred to water at such different temperature, can be found only if the weight of a like volume of water at the same temperature as that of the liquid be first ascertained, either by actual experiment or by reference to the subjoined table.

WEIGHT OF 1 CUBIC CENTIMETER OF DISTILLED WATER AT DIFFERENT TEMPERATURES.

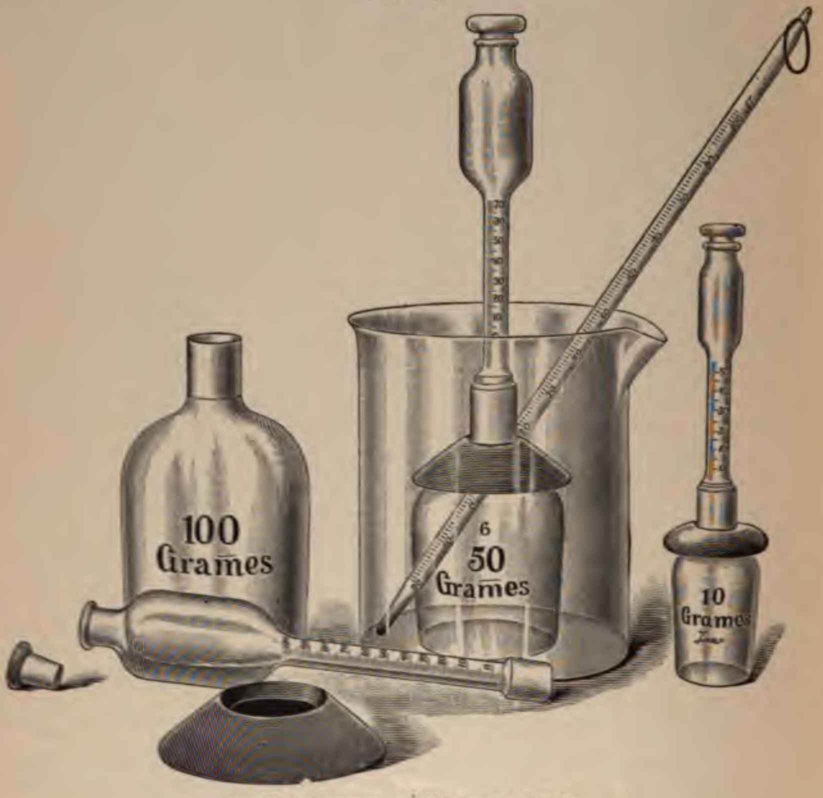
At 0° C.	= 0.99988 Gramme.	At 18° C	= 0.99866 Gramme.
1°	= 0.99993	19°	= 0.99848
2°	= 0.99997	20°	= 0.99827
3°	= 0.99999	21°	= 0.99806
4°	= 1.00000	22°	= 0.99785
5°	= 0.99999	23°	= 0.99762
6°	= 0.99997	24°	= 0.99738
7°	= 0.99993	25°	= 0.99714
8°	= 0.99989	30°	= 0.99579
9°	= 0.99982	35°	= 0.9944
10°	= 0.99974	37°	= 0.9934
11°	= 0.99965	40°	= 0.9924
12°	= 0.99955	45°	= 0.9904
13°	= 0.99943	50°	= 0.9881
14°	= 0.99930	60°	= 0.9833
15°	= 0.99915	70°	= 0.9778
15.5°	= 0.99908	80°	= 0.9718
16°	= 0.99900	90°	= 0.9656
17°	= 0.99884	100°	= 0.9586

The following examples will serve to illustrate the usefulness of the table:

If a bottle graduated to hold 25 grammes of distilled water at 4° C. is found to hold 27.5 grammes of another liquid at 25° C., the U. S. Pharmacopœial standard temperature, what will be the specific gravity of that liquid at $\frac{25^\circ}{25^\circ}$ C.? By reference to the table we find that a cubic centimeter of water weighs 1.0 gramme at 4° C., but only 0.99714 gramme at 25° C.; hence a volume of water which weighs 25 grammes at 4° C. will weigh $\frac{99714}{100000}$ of 25 grammes at 25° C., or 25×0.99714, which is equal to 24.9285 grammes. Applying the rule for finding specific gravities, and dividing 27.5 by 24.9285, we have 1.103+ as the specific gravity of the liquid at $\frac{25^\circ}{25^\circ}$ C.

What will be the specific gravity of a liquid according to the official standard, $\frac{25^\circ}{25^\circ}$ C., if found to be 1.310 at $\frac{25^\circ}{15.5^\circ}$ C.? As the specific gravity was found by dividing the weight of the liquid at 25° C. by the weight of an equal volume of water at 15.5° C., each cubic centimeter of the liquid must have weighed 1.3087948 grammes, since the liquid appears 1.31 times as heavy as water, and 1 cubic centimeter of water weighs 0.99908 gramme at 15.5° C., as stated in the table. A cubic centimeter of water at 25° C., however, weighs 0.99714 gramme, and as a cubic centimeter of the liquid at the same temperature has been found to weigh 1.3087948 grammes, the specific gravity at $\frac{25^\circ}{25^\circ}$ C. must be 1.3125 +, for 1.3087948 divided by 0.99714 is equal to 1.3125 +.

Fig. 30.



Squibb's improved specific gravity bottles.

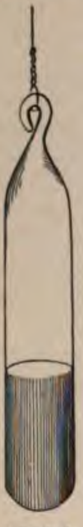
With the view of overcoming the difficulties usually encountered in regard to temperature, and of insuring more accurate results, the late Dr. E. R. Squibb had constructed a set of specific gravity bottles which are equally well adapted for measuring accurately the standard water volume at any temperature from 0° C. to 25° C., and in which liquids can without loss be brought to room-temperature (or even 25° C., 77° F.) for weighing (see Fig. 30). As seen in the illustration, the bottles may be made of such size as to hold any desired weight of distilled water. They are provided with a long, narrow tube stopper graduated into ½ millimeters from 0 to 50 or 100, to which is attached a safety reservoir fitted with a ground-glass stopper. The capacity of the bottles is so adjusted that the prescribed weight of recently boiled distilled water will reach to the 0 mark, or a little above it, when the bottle and contents have been kept in a bath of melting ice at 0° C. (32° F.) for fifteen minutes or until the volume ceases to recede. The height to which this same weight of distilled water will rise in the graduated tube at any higher temperature can be readily ascertained by immersing the bottle and contents in a water-bath kept at the desired temperature until the column ceases to rise. By keeping a memorandum of the height of the column in ½-millimeter divisions to which the prescribed weight of distilled water will rise at any stated temperature, an equal volume of any other liquid at the same temperature may readily be obtained, accurate adjustment being made by means of very narrow strips of blotting-board passed down the bore of the graduated stem for the purpose of absorbing and removing minute quantities of liquid. Having found the weight of such a volume of any liquid, the specific gravity of that liquid, as compared with water at the same temperature, can be quickly ascertained by dividing the weight found by the prescribed weight of water.

Since glass bottles contract appreciably for two years or more after they have been made, the graduations should be verified every six months or more until contraction has ceased, a memorandum of the changes being kept for reference when the bottle is to be used; thus the point for the volume at 4° C. may have advanced 2 or 3 divisions of the scale, and similarly for any temperature volume. The bottles are always used in a bath of either warmed or cooled water, and when the volume does not change for five minutes, as indicated by the graduated scale, the contents of the bottle may be known to have assumed the temperature of the bath as ascertained by means of a delicate thermometer. A leaden collar is used to keep the bottles steady in the bath.

Besides taking the specific gravity of liquids by means of a pycnometer, accurate results may also be obtained with the so-called loaded cylinder. Its use is based on the law formulated by Archimedes, a Greek philosopher, that all bodies immersed in a liquid are buoyed up with a force equal to the weight of the liquid displaced by them, and thus appear to lose weight. For instance, a piece of metal the size of 1 cubic inch, when immersed in water, will exert as much less pressure on the bottom of the container as will equal the weight of 1 cubic inch of water—a fraction over 252 grains—and hence will weigh 252 grains less in water than in air. Floating bodies always displace their own weight of water irrespective of their volume, while immersed bodies always displace their own volume of water irrespective of their weight. All bodies, therefore, which weigh less than an equal volume of water are sure to float in that liquid, only so much of the body being immersed as corresponds in volume to a weight of water equal to the weight of the whole body; on the other hand, all bodies weighing more than an equal volume of water must sink in that liquid and be completely immersed, as the downward pressure of the body exceeds the upward pressure or buoyant force of an equal volume of water.

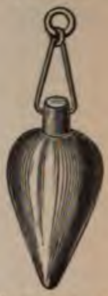
The loaded cylinder, as shown in Fig. 31, consists of a glass tube partly filled with mercury, and sealed at the top, to which is affixed a hook for convenient suspension to a scale beam. Having weighed the cylinder in air and then in pure water, at any given temperature, the weight of an equal volume of water is ascertained by subtracting the weight in water from the weight in air; the cylinder is then weighed in any desired liquid at the same temperature as the water, and the loss in weight again noted, which is the weight of an equal volume of that liquid. The volume of the liquid to be tested, being equal to the volume of the cylinder, must be equal to the volume of water also, for things that are equal to the same thing are equal to each other; by dividing the weight of the given volume of the liquid by the weight of the same volume of water, the specific gravity of the liquid is obtained. Example: A loaded cylinder weighs in air 150 grains, and in water 120 grains, loss of weight in water 30 grains; immersed in sulphuric acid it weighs 96 grains, showing a loss of 54 grains; equal volumes of the acid and water weighing 54 and 30 grains respectively, the specific gravity of the acid must be 1.800, for 54 ÷ 30 = 1.8.

FIG. 31.



Loaded cylinder.

FIG. 32.

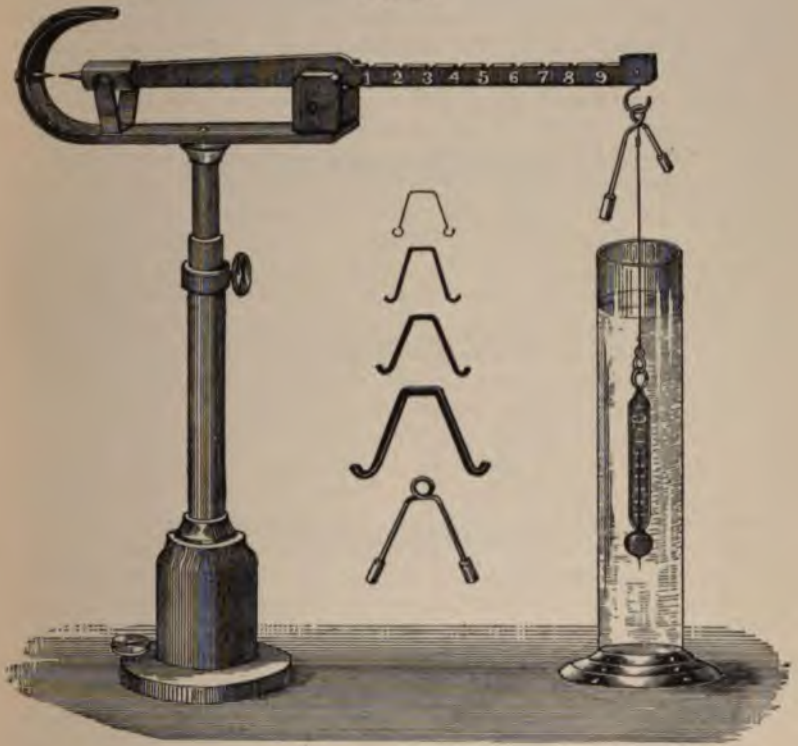


Glass or metal plummet.

When only a small quantity of liquid is available for taking the specific gravity the loaded cylinder may be replaced by a small glass or platinum weight of the shape shown in Fig. 32; or Grauer's method may be followed. This consists in using a small pipette having a fine orifice at one end, and at the upper end a short piece of rubber tubing closed by a pinchcock; a mark is made on the glass stem, showing the height to which a convenient quantity of water rises (say 1.0 Gm. or 1.0 Cc.), and enough of the liquid to be tested is drawn up through the tube to the mark previously made, the tube is closed, and the whole then weighed; the weight of the liquid in grammes expresses the specific gravity with sufficient accuracy for all practical purposes, as water increases its volume from 4° to 100° C. only to the extent of 0.012, or about $\frac{1}{84}$.

The principle of the loaded cylinder has been utilized in the construction of the Mohr specific gravity balance, of which the Westphal modification is a most desirable improvement (see Fig. 33). The specific gravity of a liquid can be quickly taken at any temperature between 7° and 30° C., since the loaded cylinder has been replaced by a short glass thermometer, which is suspended from the end of the beam by a thin platinum wire; the adjustment having been made at 15° C., a slight variation will be observed for any higher or lower temperature. The small thermometer has a range of twenty-three degrees on the centigrade scale, and, when suspended in air from the longer arm of the beam, establishes perfect equilibrium; when completely immersed in distilled water at 15° C. it displaces its own volume of the water and is buoyed up by a force equal to the weight of the water displaced—equilibrium of the beam being re-established by attaching the necessary counterpoise, which is called 1.000: at 7.5° C. the necessary weight was found to be 1.001, while at 27° C. it was 0.998. As seen in the illustration, the

Fig. 33.



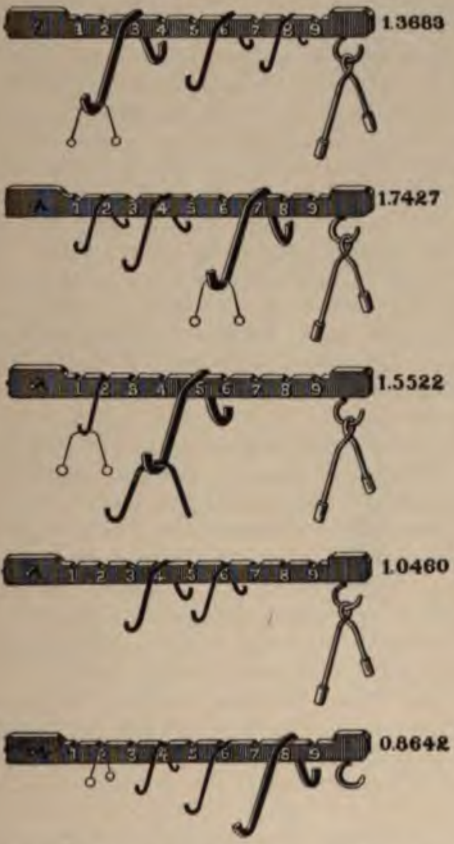
The Westphal specific gravity balance.

longer arm of the beam is accurately divided into ten even spaces, and the weights, or riders, used to counterbalance the thermometer when immersed in any liquid, are made of brass and aluminum; they are so constructed that each smaller rider is of exactly $\frac{1}{10}$ the value of the next larger, the largest rider and the counterpoise used to balance the thermometer in water, however, being of the same weight or value. Without the necessity for calculation, if the temperature of the liquid be at 15° C., the specific gravity of the liquid can be at once read off, after the equilibrium of the beam has been established; for instance, in testing alcohol at 15° C., the counterpoise necessary to balance the beam in water will be found too heavy if attached at the same point in alcohol, hence it is removed and the largest rider is placed in the first, or, if necessary, in the second notch on the beam, where it may appear a little too light, and then the smaller riders are added as may be necessary to balance the beam perfectly. The value of each of the two larger riders, when suspended from the end of the beam, is considered as 1.000, while the three smaller riders are valued at 0.100, 0.010, and 0.001 respectively; when removed to the top of the beam the value of each rider is reduced by $\frac{1}{10}$ for every notch. If one of the large riders be placed at the notch marked 8, a second rider at 2, and a smaller rider at 1, the specific gravity of the alcohol must be read as 0.821. In the case of chloroform and all other liquids specifically heavier than water, the large counterpoise is suspended from the end of the beam, and the other riders are placed in the notches as may be necessary; thus chloroform may require all four riders on the beam, the largest at 4, the second at 8, and the smaller two at 9, which would be read as 1.4899 specific gravity. Whenever two riders of different weight are required in the same notch on the beam, the lighter of the two is suspended from the hook of the heavier, as shown in Fig. 34; thus the specific gravity of liquids can be read with accuracy to four decimal places. The Mohr or Westphal balance cannot be used, however, if only very small quantities of liquid are available, as sufficient liquid is required to immerse the glass thermometer completely.

Specific gravity beads, also known as Lovi's beads, are small, sealed, pear-shaped glass bulbs of various specific weights, which have been carefully ascertained and are marked on them; these beads will float indifferently in any liquid having the same specific gravity, and may be used in adjusting liquids to a fixed specific gravity by dilution or evaporation. If a bead marked 0.93 be placed in a jar of alcohol, it will sink—unless the liquid happens to be official diluted alcohol—but will slowly rise upon the addition of water, until a sufficient quantity has been added to increase the specific gravity of the mixture to that indicated on the bead, when it will float about midway in the liquid. Results obtained with specific gravity beads are never so accurate as with other methods.

Hydrometers, or areometers, are instruments intended to indicate either the density or the specific gravity of liquids, and in some cases also the percentage by volume or weight of certain liquids. They consist of a glass tube having a bulb blown at one end, a little above which the tube is usually expanded cylindrically for a short distance, and then terminates in a long stem in which is securely fastened a graduated paper scale (see Fig. 35). The bulb is filled with mercury or small shot, so as to enable the instrument to assume a vertical position when floated in any liquid. Hydrometers, like all floating bodies, displace their own weight of a liquid and sink in it to a depth proportional to the volume of liquid displaced, which volume is equal in weight to the weight of the instrument; thus, by comparison of volumes displaced, the densities and specific gravities

Fig. 34.



Showing the manner of reading the specific gravities.

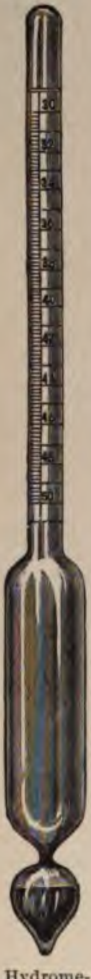
of various liquids can be ascertained. While the great majority of hydrometers are so constructed that with constant weight they will sink to varying depths in different liquids, some are made to sink to a uniform depth in all liquids by the addition or subtraction of weights, and the density or specific gravity is calculated from such change of weight; this latter class can also be conveniently used for taking the specific gravity of solids.

Specific gravity hydrometers are made with the unit mark 1.000 at a point to which the instrument sinks in distilled water at *normal temperature* (usually 15.6° C. or 60° F.), and then have the scale carried above and below this point, each mark on the scale indicating either 0.001, or 0.005, or 0.010, according to the intended delicacy of the instrument. As specific gravities of liquids range from 0.700 to above 2.00, the tube of a hydrometer carrying such a scale would have to be inconveniently long to permit of a fair reading of it; hence specific gravity hydrometers usually come in sets of four, ranging from 0.600 to 1.000, from 1.000 to 1.400, from 1.400 to 1.800, and from 1.800 to 2.200. When intended for testing the specific gravity of special liquids the scale is usually much shorter, and thus permits of more accurate graduation.

By far the larger number of hydrometers are intended for determining the density of liquids irrespective of specific gravity; they are extensively employed for technical purposes, and are based on arbitrary scales, no two of which agree, but which can be converted into specific gravity by certain rules. To this class belong Baumé's, Twaddell's, Cartier's, Zanetti's, Sikes', Beck's, Jones', and other hydrometers. Since Baumé's hydrometers are largely used by manufacturing chemists in this country, and the *degrees Baumé* are often stated on labels, the instrument is of special interest to pharmacists.

Baumé devised two hydrometers, one for liquids heavier than water and the other for liquids lighter than water; the former was called *Pèse-Acide*, or *Pèse-Sirop*, and the latter *Pèse-Esprit*. For liquids heavier than water the zero was placed at the point to which the instrument sank in distilled water at 15.6° C., and the point to which it sank in a solution of 15 parts of dry table salt and 85 parts of distilled water, also at 15.6° C., was marked 15; the distance between these two points was then divided into 15 equal parts, called *degrees*, and the scale extended as far as the length of the tube would permit. The zero for liquids lighter than water was found by immersing the instrument in a solution of 10 parts of dry table salt and 90 parts of distilled water at 15.6° C. in such a way that

FIG. 35.



Hydrometer, plain.

the long stem would be almost entirely out of the liquid; the point to which the instrument sank in distilled water, also at 15.6° C., was marked at 10, the space between the two points being divided into 10 equal parts and the scale extended as in the other case. The slightest error in obtaining the first interval is increased upon extension of the scale; hence it is almost impossible to find two instruments adjusted by the old method to correspond exactly. A more accurate and equally practicable method is to obtain the exact specific gravity of two liquids compared with distilled water at a fixed temperature, place these at the extremes of the scale, and then divide the intervening space into the requisite number of degrees. The liquids chosen in this country, for liquids heavier than water, are concentrated sulphuric acid having the specific gravity 1.8354 at 15.6° C., and distilled water; and for liquids lighter than water, highly rectified ether having the specific gravity 0.725 at 15.6° C., and distilled water; the space between the points to which the hydrometer sinks in the water and the acid is divided into 66 parts, or degrees, and the space between the points to which it sinks in the ether and the water into 53 parts. For all liquids heavier than water the scale is read from above downward, while for liquids lighter than water it is read from below upward (see Figs. 36 and 37).

Fig. 36.

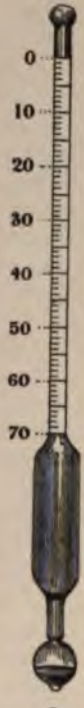
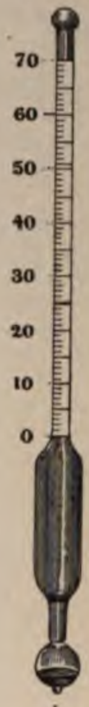


Fig. 37.



Baumé's hydrometers. *a*, for liquids heavier than water; *b*, for liquids lighter than water.

As it is frequently desirable to know the specific gravity for any given degree on the Baumé scale, and *vice versa*, the following rules have been formulated.

For liquids heavier than water: Subtract the degree Baumé from 145 and divide the remainder into 145 to find the specific gravity.

Divide 145 by the specific gravity and subtract the quotient from 145 to find the degree Baumé.

For liquids lighter than water: Add the degree Baumé to 130 and divide the sum into 140 to find the specific gravity.

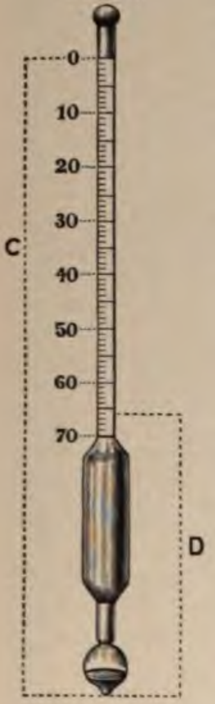
Divide 140 by the specific gravity and from the quotient subtract 130 to find the degree Baumé.

The moduli or constants employed in these rules which express the proportion borne by the weight of water displaced by the hydrometer when floating in water, to the weight of water equal in volume to one degree, are deduced as follows:

Case I. For Liquids Heavier than Water.—Let a = specific gravity of the lighter liquid, b = specific gravity of the heavier liquid, c = volume of the lighter liquid displaced, and d = volume of the heavier liquid displaced.

The difference between the volumes of the two liquids displaced, as seen in Fig. 38, is $c - d$, indicated by the degrees on the scale to which the hydrometer sinks in the heavier liquid; and hence d, representing the volume of heavier liquid displaced, must be equal to c — the number of degrees.

FIG. 38.



The object, first, is to find what relation the volume displaced by the instrument when immersed in water bears to the volume of one degree on the graduated scale, taken as the unit—that is, to find how many degrees on the scale the total volume, c, of lighter liquid displaced, is equal to. The discussion of specific gravity has already shown that the weight of any body is equal to the product of its volume by its specific gravity; hence the weight of water displaced by the hydrometer is equal to the volume displaced multiplied by the specific gravity of water, or equal to $c \times a$; and the weight of heavier liquid displaced is equal to the volume displaced multiplied by its specific gravity, or equal to $d \times b$.

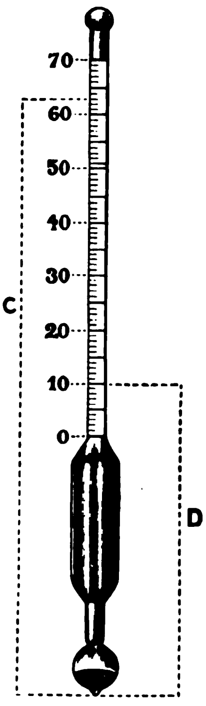
From the law of floating bodies (see p. 54) we know that the weights of the two liquids displaced are the same, being equal to the weight of the hydrometer; and hence it is evident that $c \times a = d \times b$, or $a \times c = b \times d$. Substituting the value of d, as found above, in the equation, we get $a \times c = b \times (c - \text{number of degrees})$, which is equal to $ac = bc - (b \times \text{number of degrees})$. Transposing, we get $-bc + ac = -b \times \text{number of degrees}$, or $bc - ac = b \times \text{number of degrees}$; and factoring, $(b - a)\,c = b \times \text{number of degrees}$, from which it follows that $c = \dfrac{b \times \text{number of degrees}}{b - a}$.

As already stated, distilled water and sulphuric acid of 1.8354 specific gravity are the liquids now used in adjusting hydrometers for liquids heavier than water; and the following numerical values, $a = 1.000$, $b = 1.8354$, number of degrees $= 66$, can therefore be substituted in the formula just found, when it becomes $c = \dfrac{1.8354 \times 66}{0.8354}$, or $c = 145$, which means that the volume of water displaced by the hydrometer, c, is 145 times as great as the volume corresponding to 1 degree on the graduated scale. The ratio between the two volumes therefore is 145.

The rule for converting the degrees on the hydrometer into specific gravity may be arrived at in the following manner: For equal weights of two substances, the volumes are inversely proportional to the specific gravities. This can be seen from the equation deduced above, viz., $c \times a = b \times d$, which gives the proportion $c : d :: b : a$, since the product of the extremes is equal to the product of the means. From the equation we deduce $b = \frac{c \times a}{d}$, or, since $a = 1$, $b = \frac{c}{d}$; and since $d = c -$ number of degrees, $b = \frac{c}{c - \text{number of degrees}}$. As the value of c has been found to be 145, the specific gravity of the heavier liquid $= \frac{145}{145 - \text{number of degrees}}$.

Case II. For Liquids Lighter than Water.—In finding the modulus for hydrometers intended for liquids lighter than water, a slight modification is necessary, as water in this case is the heavier liquid, and consequently a smaller volume of it will be displaced by the instrument. It must also be borne in mind that on the scale for liquids lighter than water the point to which the hydrometer sinks in water has been fixed at 10 degrees, instead of at 0. As in Case I., let $a =$ specific gravity of the lighter liquid, $b =$ specific gravity of the heavier liquid, $c =$ volume of the lighter liquid displaced, $d =$ volume of the heavier liquid displaced.

FIG. 39.



By proceeding precisely as in the previous case, we arrive at the same equation, viz., $c \times a = d \times b$ or $a \times c = b \times d$. Hence d, the volume of water displaced, $= \frac{c \times a}{b}$.

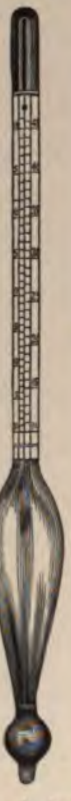
As may be seen in Fig. 39, $c - d$, the difference between the volumes of lighter liquid and water displaced, is expressed by the number of degrees difference between the point to which the hydrometer sinks in the lighter liquid and 10, since the water level is at the latter point. The volume of lighter liquid displaced, therefore, is equal to d (the volume of water displaced) plus the difference between c and d—that is, $c = d + (c - d)$.

Replacing the value of c in the equation $d = \frac{c \times a}{b}$, we have $d =$

$\frac{(d+(c-d))\times a}{b}$, from which we get $bd = ad + (c-d)a$. Transposing we have $bd - ad = (c-d)a$, and by factoring $(b-a)d = (c-d)a$; hence $d = \frac{(c-d)a}{(b-a)}$.

As highly rectified ether and distilled water are used in the adjustment of hydrometers for liquids lighter than water, the following numerical values, $a = 0.725$, $b = 1.000$, $c - d = 53$, can be substituted in the equation, and we obtain $d = \frac{53 \times 0.725}{0.275}$, or $d = 139.7$, which means that the volume of water displaced by the hydrometer bears a ratio of 139.7 to the volume corresponding to 1 degree on the graduated scale; but since the use of 139.7 as the modulus or constant would involve undesirable fractions in applying the rule for conversion into specific gravity, the number 140 has been accepted as the equivalent of d. It is readily seen from the figure that the volume of water displaced by the hydrometer up to the zero mark is $d - 10$ degrees—that is, $140 - 10$, and that c, the volume of lighter liquid displaced, will always be the volume displaced up to the zero mark plus the number of degrees to which the instrument sinks in the lighter liquid—that is, $(140 - 10) +$ the number of degrees, or $130 +$ the number of degrees.

FIG. 40.



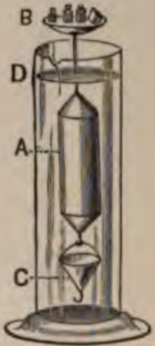
Double hydrometer for density and specific gravity determinations.

The rule for converting the degrees on hydrometers for liquids lighter than water into specific gravity, is also deduced from the regular equation $c \times a = d \times b$, or $a = \frac{d \times b}{c}$. Having found numerical expressions for b, c, and d, the formula becomes $a = \frac{140 \times 1.000}{130 + \text{the number of degrees}}$; or the specific gravity of the lighter liquid is obtained by dividing 140 by 130 plus the number of degrees to which the hydrometer sinks.

In order to avoid the use of rules and tables in connection with arbitrary scales, hydrometers have been in use for some years bearing a double scale, for Baumé degrees and the corresponding specific gravity, as shown in Fig. 40: they come in sets, usually five, two of which are intended for liquids lighter than water, and three for liquids heavier than water, the shorter size permitting closer reading within smaller limits.

The Twaddell hydrometer is only for liquids heavier than water, each degree on the scale being equal to 0.005 specific gravity; hence the requisite number of degrees multiplied by 0.005 and added to 1.000 expresses the specific gravity of any liquid; thus, if a sample of glycerin stands at 50° Twaddell, its specific gravity will be 1.250, for $50 \times 0.005 = 0.25$, and $1.000 + 0.25 = 1.250$.

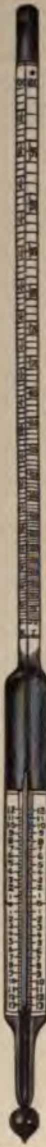
FIG. 41.



Nicholson's hydrometer.

Nicholson's hydrometer is of the kind intended to sink to a uniform depth (indicated by a mark on the stem) in all liquids by the use of weights, and also possesses the advantage that it can be used for finding the specific gravity of solids as well as liquids. Fig. 41 represents a Nicholson hydrometer floating in a liquid. The construction is readily explained: A is an elongated glass or metal bulb, terminating in a stem surmounted by a metallic disk, B; on the stem is a mark at D, indicating the point to which the instrument must be made to sink; and attached to the bottom of the bulb, by means of a small hook, is a loaded cup, C, with finely perforated sides, for carrying solids if so desired. The weight of the instrument complete is marked on the same by the manufacturer, and frequently also the weight which must be placed on the disk B in order to float the hydrometer at D in distilled water. When the latter is omitted, as is sometimes the case, it becomes necessary to ascertain the weight of the volume of water displaced by the hydrometer when immersed to D in distilled water; this is done by placing sufficient weights on the disk to enable the instrument to float at D, and then adding such weights to the known weight of the hydrometer; the sum will represent the weight of water displaced. The weights necessary to sink the instrument to the point D in different liquids when added to the weight of the hydrometer therefore represent the weights of equal volumes of such liquids; hence the sum of weights needed for any one liquid divided by the weight of an equal volume of distilled water at the same temperature will express the specific gravity of that liquid. To find the specific gravity of a solid body, first ascertain the weight of the solid body in air by placing it on the pan B, and then, having floated the instrument in distilled water, adjusting the weights necessary to sink the hydrometer to D; the difference between the weight required to sink the hydrometer to D in water, without and with the solid body on the metal disk B, indicates the weight of the solid body in air. Now place the solid body in the cup C and again adjust the weight; the difference between the present weight and that required when the solid body was on the disk expresses the weight of the water displaced by the solid body; or, in other words, the weight of water equal in volume to the solid body. Finally, divide the weight of the solid body in air by the loss of weight in water, and the quotient will express the specific gravity of the solid body. If the solid body should be lighter in water, and hence float in the same, the cup C must be inverted and attached to the elongated bulb by means of the small stirrup under the cup, so that the solid body may be placed underneath of the cup and thus be kept immersed. Solid bodies soluble in water must, of course, be tested in a liquid in which they are wholly insoluble and the specific gravity of which has previously been determined; the calculations for this method are explained on page 68.

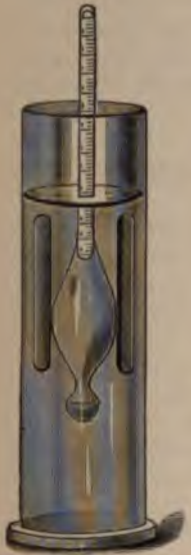
FIG. 42.



Alcoholometer with thermometer enclosed.

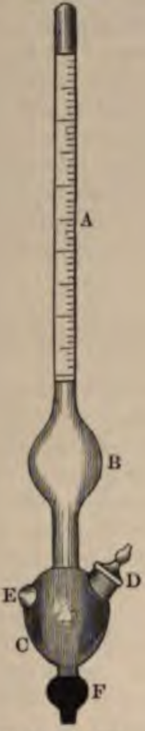
Spirit hydrometers, usually called alcoholometers, are used to ascertain the percentage of absolute alcohol in the commercial article; since the value of alcohol depends entirely upon the amount of absolute alcohol present, this instrument is a most desirable piece of apparatus for pharmacists. Alcoholometers are made of glass, like ordinary hydrometers, but of much longer shape, and are usually provided with two separate scales—Richter's scale, indicating the percentage of alcohol by weight, and Tralles' scale, showing the percentage by volume; since the instrument is adjusted at 60° F. (15.6° C.), it becomes necessary to make proper corrections for any variations in temperature. When immersed in alcohol at normal temperature the figures on the respective scales to which the instrument sinks indicate the number of parts of absolute alcohol contained in 100 parts of the specimen, the lowest mark on the scale being 0, to which the hydrometer will sink in pure water. Since a cold temperature, by contraction, increases the density of alcohol, the instrument cannot sink as low in the liquid if the temperature be below 60° F. (15.6° C.) as when at 60° F. (15.6° C.); an additive correction in the reading of the scale must therefore be made. On the other hand, if the temperature rise above 60° F. (15.6° C.), the density of the alcohol will decrease and the hydrometer will sink lower, hence a subtractive correction must be made for temperature. The necessary correction has been ascertained to amount to 0.15 for every degree above 60° on the Fahrenheit scale, or 0.27 for every degree above 15.6° on the centigrade scale. For example, if an alcoholometer sinks in alcohol to 93 on the Tralles' scale at 50° F. (10° C.), the liquid contains really 94.5 per cent. of absolute alcohol by volume, instead of 93 as indicated on the scale, for the temperature is 10 degrees below the normal (60° F.), hence 10×0.15, or 1.5, must be added; but if the temperature had been 70° F. (21.11° C.), the true percentage of alcohol by volume would have been only 91.5, for, the temperature being 10 degrees above the normal, a subtraction of 1.5 from the reading 93 is necessary.

Fig. 43.



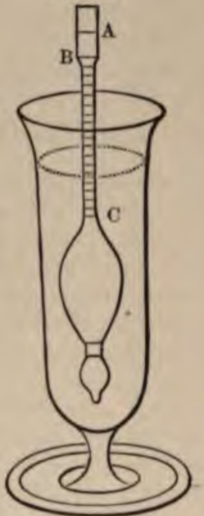
Squibb's urinometer and cylinder.

Fig. 44.



Eichhorn's areopycnometer.

Fig. 45.



Rousseau's densimeter.

Fig. 42 represents a complete alcoholometer carrying a thermometer within the tube for convenience in taking the temperature of the liquid. For testing the specific gravity of urine, a small hydrometer the range of which extends from 1.000 to 1.060 is employed (see Fig. 43); the narrow cylinder in which to float the urinometer was specially designed by Dr. Squibb with the view of preventing the hydrometer from adhering to its sides, by means of the peculiar indentations.

Special instruments have been devised for taking the specific gravity of very small quantities of liquids, namely, Eichhorn's areo-pycnometer (Fig. 44) and Rousseau's densimeter (Fig. 45): instead of floating these instruments in the liquid to be tested, the latter is carried in the hydrometer, which is then floated in water. The illustration of the areo-pycnometer shows that it differs in construction from the ordinary hydrometer chiefly in having a glass bulb, C, placed between the loaded bulb F and the expanded portion B of the stem; the bulb C is provided with a stopcock, D, and into it is poured the fluid to be tested; the small glass knob E serves to balance the instrument when immersed in water, which should be at 17.5° C. (63.5° F.); the specific gravity is shown on the graduated scale on the tube A. The densimeter is chiefly intended to be used for oils and similar liquids lighter than water. The upper part of the tube, A to B, consists of a little cup of 1 Cc. capacity; when floated in water the instrument sinks to the point C, and when carrying 1 Cc. of water in the cup it sinks to B. The space on the stem between B and C is divided into 20 equal parts, each division corresponding to $\frac{1}{20}$ Gm. or 0.050 Gm.; now, if 1 Cc. of oil of peppermint be poured into the cup and the instrument floated in water, it will probably sink to the eighteenth division of the scale; hence $18 \times 0.05 = 0.900$, the specific gravity of the oil.

SPECIFIC GRAVITY OF SOLIDS.

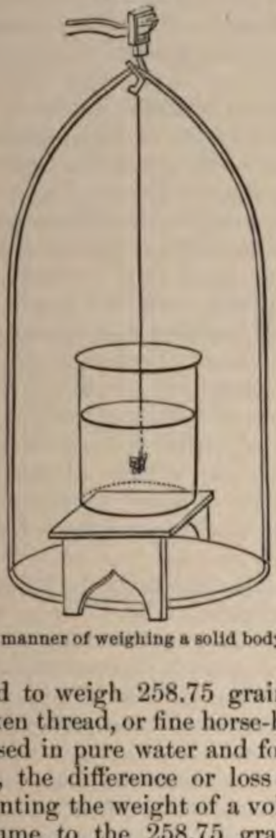
The various methods for finding the specific gravity of solids are based upon the well-established principles that all bodies immersed in a liquid displace a quantity of that liquid equal in volume to the volume of the body immersed, and at the same time are buoyed up with a force equal to the weight of the liquid displaced. The upward pressure exerted by the liquid upon the body immersed causes the latter to appear lighter in weight, and is proportional to the density of the liquid; the loss of weight, then, which a body seems to suffer upon immersion in any liquid represents the weight of a volume of that liquid identical with the volume of the body immersed. As stated on page 47, pure water at 25° C. (77° F.) has been chosen as a standard of comparison for solids, and may be directly employed for the immersion of all bodies upon which no solvent effect is produced; in the contrary case other liquids must be used, as will be shown later on. The specific gravity of any solid can be ascertained by the simple rule of three, provided the first three terms of the proportion are known, namely, first term, the weight of the liquid displaced; second term, the weight of the solid in air; third term, the specific gravity of the liquid used for immersion. Whenever water is used for immersion, the simple division of the weight of the solid in air by the loss of weight in water (weight of water displaced) expresses the specific gravity of the solid, since the specific gravity of water is 1.000. The methods for finding the specific gravity of solids may be divided as follows:

1. For solids insoluble in, but heavier than water;
2. For solids insoluble in, but lighter than water;
3. For solids soluble in water, whether heavier or lighter than that liquid;
4. For solids in powder form.

For solids insoluble in, but heavier than water, several methods are available; of these, the direct method of weighing is the most accurate and generally employed.

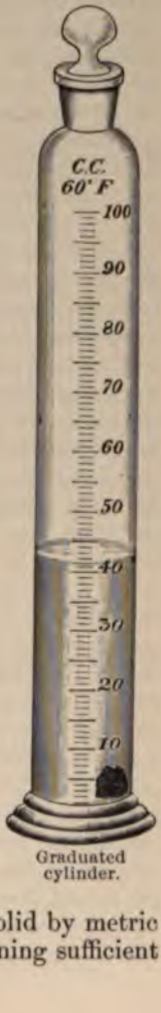
In place of the more expensive hydrostatic balance, any good sensitive prescription balance may be used; the only extra piece necessary being a small wooden or stiff wire bench as a support for the vessel of water, as shown in Fig. 46. For instance, a piece of metal is found to weigh 258.75 grains in air; by means of a silken thread, or fine horse-hair, it is completely immersed in pure water and found to weigh 235.75 grains, the difference or loss of weight, 23 grains, representing the weight of a volume of water equal in volume to the 258.75 grains of metal. Dividing 258.75 by 23, the specific gravity of the metal is found to be 11.25.

Fig. 46.



Showing the manner of weighing a solid body in a liquid.

Fig. 47.



Graduated cylinder.

Another but less accurate method is to weigh the solid by metric weight and then place it in a graduated cylinder containing sufficient water to submerge the solid completely (see Fig. 47); the difference between the first height of the water and that after immersion of the solid indicates the volume of water displaced, and its corresponding weight is readily noted. Suppose a solid body weighing 7.5 Gm., placed into 40 Cc. of water, causes the latter to rise to 41.5 Cc., showing that 1.5 Cc. of water have been displaced, which weighs 1.5 Gm.; then, applying the rule, $7.5 \div 1.5 = 5$, the specific gravity of the solid.

Since solid bodies will float indifferently in any liquid having the same specific gravity as their own, advantage may be taken of this property to determine the specific gravity of solids. Hager recommends determining the specific gravity of fats by placing them in alcohol and then adding water until the fat floats about indifferently beneath the surface of the mixture; the specific gravity of the mixture is then taken in the usual way, preferably by means of a pycnometer, and this at the same time expresses the specific gravity of the solid.

To ascertain the specific gravity of solids insoluble in, but lighter than water, it becomes necessary to insure their immersion in water by attaching to them some heavy substance, the weight of which in water must previously have been ascertained. Upon immersing the two bodies in water it will be observed that the weight of the two appears less than the weight of the heavy body alone, which is due to the fact that the volume of water equal to the volume of the lighter body is heavier than the latter, and therefore exerts a greater upward pressure on the heavy body, causing it to appear to lose weight. The difference between the weight of the heavy body in water and the united weight of the light and heavy bodies in water expresses the excess of weight of a volume of water over the weight of a like volume of the light body; in other words, it shows how much heavier a volume of water is than the same volume of the light body; to find the exact weight of a volume of water equal to the volume of the light body, this difference, or excess, must be added to the weight of the light body in air. Suppose a piece of cork weighs 62.5 grains in air; attached to a piece of metal which weighs 94 grains in water, the whole is found upon immersion in water to weigh 88 grains, or 6 grains less than the metal alone; adding 6 to 62.5 grains (the weight of the cork) we obtain 68.5 grains, the weight of the water displaced by the cork. The specific gravity of the cork is found by dividing 62.5 by 68.5, according to the general rule on page 49. The answer will be 0.9124+.

For solids soluble in water some other liquid must be selected for immersion, in which the solid body is perfectly insoluble and of which the specific gravity is known; in other respects any of the preceding methods may be followed. In such cases the weight of the liquid displaced, having been ascertained, may be used to find the weight of a corresponding volume of water, and the latter then be divided into the weight of the solid; or the weight of the solid in air may be divided by the weight of the liquid displaced and the quotient then multiplied by the specific gravity of the liquid; by either method the specific gravity of the soluble substance will be obtained. To find the weight of a corresponding volume of water, divide the weight of the liquid displaced by its specific gravity, for the weights of equal volumes of two bodies are to each other directly proportional as their specific gravities. Example: A piece of alum weighs 125 grains in air; immersed in oil of turpentine having the specific gravity 0.860 it weighs 62 grains; 125 divided by 63 (the loss of weight) yields 1.984; oil of turpentine weighing only 0.86 as much as water, 1.984 must be multiplied by 0.860, which gives 1.7062+ as the specific gravity of the alum. Or the weight of a volume of water corresponding to the volume of oil of turpentine displaced may be found by dividing 63 by 0.86, which equals 73.256, and this divided into 125, the weight of the alum in air, also gives 1.7062+ as the specific gravity of the alum.

Sometimes it is desirable to find the specific gravity of solids in powder form, as calomel, reduced iron, lead oxide, and the like; this is best done by using a flask or bottle known to hold a definite quantity of water, introducing a certain weight of the powder, and then filling with water and weighing the total contents; as two bodies cannot occupy the same space at the same time, it follows that the flask or bottle containing the powder cannot hold the same quantity of water as when empty, and this difference corresponds to the weight of water equal in volume to the powder. Suppose 100 grains of an insoluble powder are placed in a counterpoised bottle capable of holding exactly 1000 grains of water, the latter being then filled with pure water; if the total contents weigh 1088 grains, 12 grains of water have been displaced by the powder, for 1088 — 100 leaves 988, and as the bottle is capable of holding 1000 grains of water, the difference 1000 — 988 = 12 must have been displaced. Then applying the rule, 8.333 + is found to be the specific gravity of the powder, as 100 ÷ 12 = 8.333 +.

SPECIFIC VOLUME.

The term specific volume is used to define the ratio existing between the volumes of certain weights of bodies and the volume of the same weight of pure water; it is therefore the opposite of specific gravity. Specific volume is ascertained by dividing the specific gravity of a body into unity, and hence may be called the reciprocal of specific gravity; it may also be found by dividing the weight of a given volume of water by the weight of an equal volume of a liquid. Every pharmacist is aware that it will require vessels of different size to hold one pound of ether, water, glycerin, sulphuric acid, oil of turpentine, or chloroform, and it is often desirable to know in advance the volume of a given weight of a liquid. In the metric system this is a very simple operation, for the weight in grammes of any liquid multiplied by the specific volume, or divided by the specific gravity, of that liquid at once expresses the actual volume in cubic centimeters. To find, however, the volume of a given weight, avoirdupois or apothecaries', of a liquid, it becomes necessary first to ascertain the volume of a like weight of water, and then to multiply this by the specific volume, or to divide by the specific gravity of the liquid; or the given weight of a liquid may be divided at once by its specific gravity, which will yield the weight of a volume of water equal to the volume of the liquid, and then by finding the volume of such a weight of water the volume of the liquid is at once known.

Examples: If the volume of 500 Gm. of alcohol U. S. P. is desired, divide 500 by 0.816, the specific gravity of the alcohol, and the quotient 612.74 + will be the answer in cubic centimeters.

To find the volume of 8 ounces of official glycerin (apothecaries' weight) it is necessary to multiply by 480, the number of grains in 1 ounce, and then divide the product by 455.7, the number of grains in one U. S. fluidounce of water, the quotient ($480 \times 8 = 3840$; $3840 \div 455.7 = 8.427$), 8.427, represents the number of fluidounces contained in the same weight of water; 8.427 then divided by 1.246, the specific gravity of the glycerin, yields 6.7632 + fluidounces as the volume of 8 ounces, apothecaries' weight, of glycerin.

How large a bottle is required to hold 1 pound of chloroform of 1.490 specific gravity? One pound avoirdupois is equal to 7000 grains, and $7000 \div 1.490 = 4697.986$, the weight in grains of a volume of water equal to the chloroform; then $4697.986 \div 455.7 = 10.309$, or very nearly 10½ fluidounces.

How many fluidounces in 2 pounds of official ether having a specific gravity of 0.7165? Two pounds of water measure 30.72 fluidounces, and multiplying this by the specific volume, 1.3956 +, of the ether ($1.000 \div 0.7165 = 1.3956 +$), we obtain 42.87 + fluidounces as the answer.

ADJUSTMENT OF SPECIFIC GRAVITY AND PERCENTAGES.

While the adjustment of percentages in liquids as well as solids presents no difficulties, the reduction of liquids from a higher to a lower specific gravity is not quite so easily accomplished, since specific gravity is but the expression of the relation between volume and weight, and condensation of volume generally occurs as the result of a mixture of two liquids. Two very simple rules, or formulas, have been published for the adjustment of specific gravities of liquids, by volume and by weight; but absolutely accurate results are only possible when *no contraction* of volume takes place; in the majority of cases the condensation of volume is but very slight, and for ordinary purposes may be ignored. It is well known that the weights of equal volumes of two liquids are to each other directly proportional as the specific gravities of these liquids; therefore the weight of a liquid divided by its specific gravity represents a weight of water equal in volume to that liquid. It is also well known that the volumes of equal weights of two liquids are to each other inversely proportional as the specific gravities of these liquids; therefore, the volume of a liquid multiplied by its specific gravity represents a volume of water equal in weight to that liquid. The well-known process of *alligation* is admirably adapted to the adjustment of specific gravities of liquids by volume, but is unsuited to adjustment by weight. When two liquids of different specific gravities are mixed, the loss which one suffers will be balanced by the gain of the other; hence the two liquids used must be mixed in inverse proportion to that existing between the gain and loss of specific gravity and the specific gravity of the mixture; the difference between the higher specific gravity and the desired specific gravity of the mixture will therefore indicate the proportion of the liquid having the lower specific gravity; and the difference between the lower specific gravity and the desired specific gravity will indicate the proportion of the liquid having the higher specific gravity. For example, if solution of ferric chloride, specific gravity 1.520, is to be reduced to 1.387 specific gravity by addition of a weaker solution of 1.280 specific gravity, 107 volumes of the stronger must be mixed with 133 volumes of the weaker solution; or, in other words, 1 volume of the former with 1.243 volumes of the latter. It is customary to set down a problem in alligation in the following manner to facilitate comparison:

$$1.387 \left\{ \begin{array}{l|l} 1.520 & 0.107 = \text{proportion of the stronger liquid.} \\ 1.280 & 0.133 = \text{proportion of the weaker liquid.} \end{array} \right.$$

If a definite volume of the mixture is desired, the requisite volume of the stronger and weaker liquids may be ascertained by dividing the desired volume by the sum of the proportionals, and then multiplying each proportional by the quotient so obtained; thus, if 32 fluidounces are wanted, divide 32 by 0.240 (0.107 + 0.133), which yields 133.3; $0.107 \times 133.3 = 14.27$ fluidounces, the requisite volume of the stronger solution, and $0.133 \times 133.3 = 17.73$ fluidounces, the requisite volume of the weaker solution.

To adjust the specific gravity of a given weight of a liquid to a higher or lower specific gravity, the following formula may be employed:

$$x = \frac{w \times c\,(a - b)}{a\,(b - c)},$$

in which x represents the weight of the diluent, w the weight of the liquid to be diluted, a the specific gravity of the liquid to be diluted, b the desired specific gravity, and c the specific gravity of the diluent. (Whenever water is the diluent, c is made 1.000.) As stated before (see above), $\frac{w}{a}$ = weight of water equal in volume to w,

$\frac{x}{c}$ = weight of water equal in volume to x, $\frac{w+x}{b}$ = weight of water equal in volume to $w+x$. To find the value of x, the following equation, $\frac{w}{a}+\frac{x}{c}=\frac{w+x}{b}$, must be solved:

$$
\begin{aligned}
wcb + abx &= wac + acx \\
abx - acx &= wac - wcb \\
x \times a\,(b - c) &= w \times c\,(a - b) \\
x &= \frac{w \times c\,(a - b)}{a\,(b - c)}
\end{aligned}
$$

Example: How much water must be added to 250 Gm. of solution of potassa of 1.539 specific gravity in order to reduce the specific gravity to 1.036? Substituting numerical values for the letters in the above formula, we have $x=\frac{250 \times 1.000\,(1.539-1.036)}{1.539\,(1.036-1.000)}$; then $\frac{250 \times 0.503}{1.539 \times 0.036}=\frac{125.75}{0.055404}=2269.6$. Answer: 2269.6 Gm.

To make a definite weight of a liquid of definite specific gravity by mixing two liquids of known specific gravity, both being of the same kind, or one being water:

Let mw represent the desired weight of the mixture, x the weight of the diluent, y the weight of the liquid to be diluted, and a, b, c the specific gravity of the liquid to be diluted, of the mixture desired, and of the diluent, respectively. Since $x + y = mw$, and the value of x has been shown above to be

$$\frac{\text{the weight of the liquid to be diluted} \times c\,(a-b)}{a\,(b-c)},$$

the latter expression may be substituted for x in the equation, $x + y = mw$; thus $\frac{y \times c(a-b)}{a\,(b-c)} + y = mw$. This simplified is $yca - ycb + yab - yac = mw \times a\,(b-c)$, and cancelling, $y \times b\,(a-c) = mw \times a\,(b-c)$.

$$y=\frac{mw \times a\,(b-c)}{b\,(a-c)}$$

The value of y (weight of stronger liquid) having been ascertained, it is subtracted from mw, the desired weight of the mixture, to find the value of x, the weight of the diluent.

Example: If it is desired to make 10 pounds of ammonia-water of 0.960 specific gravity, from ammonia-water of 0.900 specific gravity, mix 3.75 pounds of the latter with 6.25 pounds of water; for, substituting numerical values for the letters in the above formula, the weight of the liquid to be diluted is equal to $\frac{10 \times 0.900\,(0.960-1.000)}{0.960\,(0.900-1.000)}=\frac{10 \times -0.036}{-0.096}=\frac{-0.36}{-0.096}=3.75$, and $10-3.75=6.25$.

This example may also be worked out by alligation, which method would give the proportional parts of the volume to be used of each liquid, as follows:

$$0.960\left\{\begin{array}{l|l} 1.000 & 0.060 \text{ or } 6 \\ 0.900 & 0.040 \text{ or } 4 \end{array}\right.$$

But as weight and not volume is called for, it becomes necessary to find the actual weights of the respective volumes by multiplying the latter by the specific gravities of the liquids; thus,

$$\begin{array}{r} 6 \times 1.000 = 6 \\ 4 \times 0.900 = \underline{3.6} \\ 9.6 \end{array}$$

The result shows that the mixture would produce only 9.6 parts by weight, and since 10 parts (or pounds) are wanted, the respective necessary quantities may be found by the rule of three; thus,

$$\begin{array}{ll} 9.6 : 6 \;::\; 10 : x & x = 6.25 \\ 9.6 : 3.6 \;::\; 10 : x & x = \underline{3.75} \\ & \phantom{x = {}}10 \end{array}$$

For the adjustment of percentage in alcohol (by weight or volume), in acids (by weight), and in alkali solutions (by weight), the following rules may be applied:

For reducing solutions from a higher to a lower percentage: *Multiply the given quantity by the given percentage and divide by the required percentage; the quotient will be the quantity to which the liquid must be diluted by the addition of water.* Since alcohol is frequently reduced in volume percentage, and contraction of volume invariably follows the admixture of alcohol and water, it becomes necessary, after contraction has ceased, to add sufficient water to restore the original volume of the mixture.

Examples: Reduce 4 pints (64 fluidounces) of 93 per cent. (by volume) alcohol to 65 per cent.: $64 \times 93 = 5952$, and $5952 \div 65 = 91.57$. Enough water must be added to the 4 pints of alcohol to yield, after contraction has ceased, 91.57 fluidounces.

Reduce 2 pounds of hydrochloric acid from 31.9 per cent. to 10 per cent.: 2 pounds = 32 avoirdupois ounces; $32 \times 31.9 = 1020.8$, and $1020.8 \div 10 = 102.08$. Enough water must be added to the 2 pounds of acid to bring the total weight up to 102.08 avoirdupois ounces.

Reduce 8 troy ounces of stronger ammonia-water, 28 per cent., to 10 per cent. strength: $8 \times 28 = 224$, and $224 \div 10 = 22.4$. Enough water must be added to the 8 troy ounces of stronger ammonia-water to bring the total weight up to 22.4 troy ounces.

For making a definite quantity of a solution of a certain percentage by diluting a stronger solution with water: *Multiply the required quantity by the required percentage, and divide by the higher percentage; the quotient will be the quantity of the stronger liquid necessary, and this subtracted from the total quantity required leaves the necessary quantity of water.* When volume adjustment of alcohol is made, the same precautions in regard to contraction of volume must be observed as stated in the preceding rule.

Examples: Make 1 gallon (128 fluidounces) of 60 per cent. (by volume) alcohol from alcohol of 94 per cent. (by volume): 128 × 60 = 7680, and 7680 ÷ 94 = 81.7. Answer: 81.7 fluidounces of the stronger alcohol must be mixed with sufficient water to yield, after contraction has ceased, 128 fluidounces.

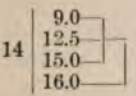
Make 4 pounds of 25 per cent. phosphoric acid from the official 85 per cent. acid: 4 pounds = 64 av. ozs.; 64 × 25 = 1600, and 1600 ÷ 85 = 18.823. Answer: Enough water must be mixed with 18.823 av. ozs. of the strong acid to bring the total weight up to 64 av. ozs.

Make 720 grains of 5 per cent. caustic potash solution from a 12.5 per cent. solution: 720 × 5 = 3600, and 3600 ÷ 12.5 = 288; 720 − 288 = 432. Answer: 288 grains of the 12.5 per cent. solution must be mixed with 432 grains of water.

The adjustment of percentage in liquids may also be readily made by the process of alligation, as already explained under adjustment of specific gravities by volume, page 71.

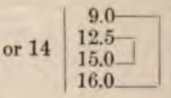
Pharmacists and drug jobbers are sometimes called upon to make mixtures of certain liquids or solids having different percentage strengths in order to produce a desired average strength; this may be done by the general rule for alligation. Write the percentages in a column, and the mean percentage on the left. Connect the simples in pairs, one less than the mean with one greater; take the difference between the mean and the numbers representing the percentage strength of each simple and write it opposite the value with which it is linked. These differences are the relative quantities of the simples taken in the order in which their values stand.

Example: In what proportion may powdered opium of 9, 12.5, 15, and 16 per cent. morphine strength be mixed to produce a mixture of 14 per cent. strength?



Proof.

$$\begin{array}{llll} 1.0 & 1 & \times 9 & = 9 \\ 2.0 & 2 & \times 12.5 & = 25 \\ 5.0 & 5 & \times 15 & = 75 \\ 1.5 & \underline{1.5} & \times 16 & = \underline{24} \\ & 9.5 & &)\,\underline{133} \\ & & & 14 \end{array}$$



Proof.

$$\begin{array}{llll} 2.0 & 2 & \times 9 & = 18 \\ 1.0 & 1 & \times 12.5 & = 12.5 \\ 1.5 & 1.5 & \times 15 & = 22.5 \\ 5.0 & \underline{5} & \times 16 & = \underline{80} \\ & 9.5 & &)\,\underline{133.0} \\ & & & 14 \end{array}$$

Answer: 1 part of 9 per cent., 2 parts of 12.5 per cent., 5 parts of 15 per cent., and 1.5 parts of 16 per cent.; or 2 parts of 9 per cent., 1 part of 12.5 per cent., 1.5 parts of 15 per cent., and 5 parts of 16 per cent.

It matters not how the simples are connected, as long as one less than the mean is compared with one greater, for while the proportional part of each simple may vary, the sum of the proportionals remains the same. If the number of simples is not evenly divided among those less and those greater than the mean, two or more of the former may be linked with one of the latter, and *vice versa;* thus, to mix 7, 8, 9, and 28 per cent. ammonia-water so as to produce 10 per cent. ammonia-water, it would be necessary to use 6 parts of the 28 per cent. solution and 18 parts each of the 7, 8, and 9 per cent. solutions.

			Proof.
10	7	18	18 × 7 = 126
	8	18	18 × 8 = 144
	9	18	18 × 9 = 162
	28	3 + 2 + 1 = 6	6 × 28 = 168
			60) 600
			10

When the number of simples is uneven, but greater than three, at least two sets of answers are possible as regards the sum of the proportionals.

If a definite quantity of one of the simples be directed to be used in the mixture, the corresponding quantities of the others are readily ascertained by multiplying their proportionals by the ratio which the given quantity bears to the proportional of the simple which it represents.

Example: How much powdered cinchona bark containing 3, 3.5, 6, and 6.5 per cent. total alkaloids may be mixed with 10 pounds of cinchona bark containing 4 per cent. total alkaloids to produce a mixed powder of official strength, 5 per cent. total alkaloids?

5	3.0	1.5
	3.5	1.5
	4.0	1.0
	6.0	1.0
	6.5	2.0 + 1.5 = 3.5

10 ÷ 1 = 10, ratio of given quantity to proportional.

Answer.	Proof.
1.5 × 10 = 15 pounds of 3 % bark.	15 × 3 = 45
1.5 × 10 = 15 " " 3.5 " "	15 × 3.5 = 52.5
1.0 × 10 = 10 " " 4 " "	10 × 4 = 40
1.0 × 10 = 10 " " 6 " "	10 × 6 = 60
3.5 × 10 = 35 " " 6.5 " "	35 × 6.5 = 227.5
	85) 425.0
	5

If a definite quantity of a mixture is required, the quantity of each simple may be ascertained by multiplying its proportional by the ratio which the total quantity required bears to the sum of the proportionals of all the simples.

Example: How many grammes of powdered opium of 9, 10, 12, 15, 16, and 17 per cent. morphine strength may be taken to produce 250 grammes of a mixture containing 14 per cent. of morphine?

14	9	3	3 × 14.706 = 44.118
	10	2	2 × 14.706 = 29.412
	12	1	1 × 14.706 = 14.706
	15	2	2 × 14.706 = 29.412
	16	4	4 × 14.706 = 58.824
	17	5	5 × 14.706 = 73.530
		17 the sum of the proportionals	250.002

250 ÷ 17 = 14.706, ratio of required quantity to the sum of the proportionals.

Answer: 44.118 Gm. of 9 per cent. opium, 29.412 Gm. each of 10 per cent. and 15 per cent. opium, 14.706 Gm. of 12 per cent. opium, 58.824 Gm. of 16 per cent. opium, and 73.530 Gm. of 17 per cent. opium.

As undesirable fractions are liable to arise in alligation, and integral numbers are always preferable, the adjustment of percentages may be made algebraically, whereby a practically unlimited number of series of correct answers may be obtained and the occurrence of fractions avoided.

Thus in the preceding example, alligation gives a series of fractional quantities which are both impracticable and open to criticism from the standpoint of absolute accuracy. To solve the problem algebraically, we can proceed as follows:

Let a represent the required quantity of opium containing 9 % of morphine.
b " " " " " " " 10 % " "
c " " " " " " " 12 % " "
d " " " " " " " 15 % " "
e " " " " " " " 16 % " "
f " " " " " " " 17 % " "

Then

$$a + b + c + d + e + f = 250; \tag{1}$$

and as the mixture is to be of 14 per cent. morphine strength,

$$\frac{.09a + .10b + .12c + .15d + .16e + .17f}{250} = .14; \tag{2}$$

clearing of fractions, we have

$$.09a + .10b + .12c + .15d + .16e + .17f = .14 \times 250, \tag{3}$$

which is equal to

$$.09a + .10b + .12c + .15d + .16e + .17f = .14\,(a + b + c + d + e + f); \tag{4}$$

transposing and subtracting, we have

$$-.05a - .04b - .02c + .01d + .02e + .03f = 0. \tag{5}$$

Since multiplying all the terms of an equation by the same number, say 100, does not alter the value of the equation, we may obtain

$$-5a - 4b - 2c + d + 2e + 3f = 0 \tag{6}$$

or

$$5a + 4b + 2c - d - 2e - 3f = 0 \tag{7}$$

In the example given we have six unknown quantities, a, b, c, d, e, and f, and but two conditions, namely, the sum of the quantities must be equal to 250 and the mean of the percentage of morphine in the six different lots is to be 14; hence any four of the unknown quantities may be said to be independent and the remaining two dependent on these four. Now if we assign arbitrary values to four of the unknown quantities, we shall be able by elimination, either by addition or subtraction, to ascertain the corresponding values of the remaining two. As the sum of the six unknown quantities is rather large, 250, it is not wise to assign very low values to any of the four quantities, as this would cause at least one of the remaining values, to be determined, to be undesirably large. If we let $a = 20$,

$b = 25$, $e = 40$, and $f = 60$, and replace these values in equation (1), we have

$$20 + 25 + c + d + 40 + 60 = 250; \tag{8}$$

transposing, we get $c + d = 250 - 20 - 25 - 40 - 60;$

hence $$c + d = 105. \tag{9}$$

Replacing now the same values in equation (7), we have

$$100 + 100 + 2c - d - 80 - 180 = 0;$$

and transposing, $2c - d = 180 + 80 - 100 - 100;$

hence $$2c - d = 60; \tag{10}$$

eliminating d by addition of equations (9) and (10), we have

$$\begin{array}{rl} c + d &= 105 \\ 2c - d &= 60 \\ \hline 3c \phantom{{}+d} &= 165 \\ c \phantom{{}+d} &= 55 \end{array}$$

If $c = 55$ and $c + d = 105$, then $d = 105 - 55$, which is equal to 50.

The number of grammes of opium to be used respectively of the six varieties may therefore be 20 of the 9 per cent., 25 of the 10 per cent., 55 of the 12 per cent., 50 of the 15 per cent., 40 of the 16 per cent., and 60 of the 17 per cent.—total, 250 grammes.

Proof: 20 at 9 per cent. = 1.8
25 " 10 " = 2.5
55 " 12 " = 6.6
50 " 15 " = 7.5
40 " 16 " = 6.4
60 " 17 " = 10.2
250 " 14 " = 35.0

The following table shows a few of the many series possible when different arbitrary values are assigned to four of the six quantities:

9%	10%	12%	15%	16%	17%		14%
4	70	30	17	44	85	=	250
15	10	60	120	20	25	=	250
6	68	32	15	36	93	=	250
6	68	32	12	42	90	=	250
4	72	12	40	74	48	=	250
20	60	40	6	44	80	=	250
24	16	46	92	32	40	=	250
10	20	78	50	40	52	=	250
24	22	40	80	44	40	=	250

CHAPTER IV.

HEAT.

ONE of the most valuable aids to the pharmacist in the numerous manipulations of the store and laboratory is **heat**; hence a knowledge of its varied application and the modes of controlling and directing its influence is necessary.

The undulatory theory regarding heat is now accepted by all scientists; this declares heat to be a force generated by the motion of the molecules of bodies, and that it is the increase or decrease of this molecular energy that gives rise to the conditions designated as *hot*, *warm*, and *cold*. No body is entirely without motion of its molecules, hence the terms heat and cold are merely relative; moreover, different bodies have different capacities for heat, as is clearly proved by two persons entering the same apartment, one of whom may complain of uncomfortable warmth, while the other experiences a chilly sensation. The chief effect of heat, or increased molecular motion, is to overcome the force of cohesion and expand the volume of bodies by increasing the intermolecular spaces; the three states of aggregation, known as solid, liquid, and gaseous, being the result of cohesive force, are, therefore, dependent upon the amount of heat generated in or applied to a body.

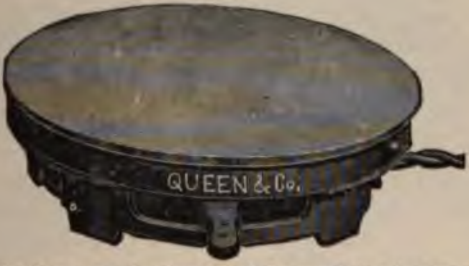
All solid bodies, when their molecular motion has become sufficiently intensified, will become luminous, as is shown by the spark emitted when steel and flint are struck together, or by the kindling of flame when two pieces of dry wood are rubbed together vigorously for some time.

Oftentimes the luminosity of heated bodies is used to indicate the degree of heat exhibited; hence such terms as dull-red heat, cherry-red heat, and white heat, of which the first named is produced during ordinary combustion of fuel in a stove, without a strong draught of air, while the last named is the result of most intense activity in molecular motion, brought about by the aid of a powerful air-blast in the combustion of fuel or by the use of electric currents.

Heat may be either active or latent; the former increases the temperature of bodies and causes their expansion, while the latter is heat hidden, after the expansion has been effected, for the purpose of keeping up the expansion. Active or sensible heat may be measured by its effect on mercury, upon which latent heat makes no impression; the latter can be converted into the former, however, by pressure and other agencies.

Heat is in almost daily use by the pharmacist in the operations of solution, fusion, evaporation, and decoction, and may be applied either by direct contact with the burning fuel or through the agency of some interposed medium. The use of coal as a fuel for the production of steam is confined to manufacturing establishments, the retail pharmacist finding illuminating-gas or some of the various kinds of coal-oil better adapted to his wants. Wherever illuminating-gas is available it is decidedly the most desirable fuel at the present day, not only because its supply is constant, but also because with modern apparatus and appliances it can be kept completely under control, and thus the greatest amount of heating power be obtained at a minimum of cost. In the course of time electricity will no doubt become an active competitor of gas for heating purposes in pharmaceutical laboratories, as its use in the arts and for domestic purposes has already demonstrated. Fig. 48 illustrates an electric plate-stove, simple in construction and very convenient for boiling and distilling inflammable liquids.

FIG. 48.



Electric plate-stove, showing switch for regulating the current.

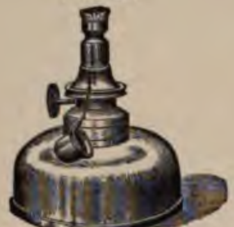
Gasoline vapor and kerosene are extensively employed for the generation of heat in localities where illuminating-gas cannot be procured; although both are quite cheap in price, a certain element of danger attends the use of the former, while the latter is open to the objections that it cannot be burned without the aid of a wick, that its flame deposits soot unless the wick is carefully watched, and that its combustion is frequently accompanied by a more or less disagreeable odor. For small operations alcohol offers an excellent fuel of good heating capacity; its high price forbids its more extensive use.

The *amount of heat* produced by the combustion of any particular fuel is constant, no matter how the combustion is effected; but the *intensity of heat* is dependent upon the rapidity of combustion; therefore, the finer the division of the fuel, the more rapidly will it be burned or oxidized, and consequently the greater will be the degree of heat generated.

Various appliances have been designed for the production of heat for pharmaceutical purposes, of which a few are shown herewith, as it is assumed that either gas or coal-oil is available everywhere.

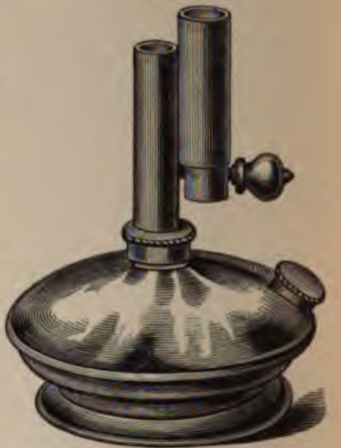
When the price of alcohol is not an object, this fuel is preferable to coal-oil where illuminating-gas is not available. Fig. 49 represents a very convenient form of spirit lamp, nickel-plated and provided with a regulating screw for the wick; it is not easily upset, and answers well for small operations at the dispensing counter.

Fig. 49.



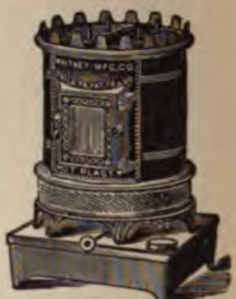
Nickel-plated spirit lamp.

Fig. 50.



Barthel's alcohol lamp.

Fig. 51.



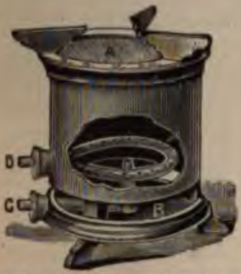
Whitney's coal-oil stove. (Single burner.)

Barthel's alcohol lamp, Fig. 50, was introduced in Germany in 1891, and is capable of producing an intense heat by the combustion of alcohol vapor. This lamp, which is perfectly safe, is extensively used in Europe; it is made of metal, has a lateral capped orifice for filling, and bears a central tube, closed on top, which carries a solid wick. This is not itself ignited, but only serves to draw up alcohol from the reservoir. To the wick-tube is attached a second tube, the burner-tube proper, which receives the vapors from the wick. The burner-tube contains a wire diaphragm, which can be raised or lowered by means of the regulating screw, and thus a higher or lower flame obtained as desired. When the lamp is to be used, the wick-tube must be heated slightly by means of a lighted match, so as to drive some alcohol vapor into the burner-tube, where it is then ignited. It will then continue to draw up alcohol vapor of its own accord. The efficiency of the lamp is shown by the fact that a quart of water can be raised from 15° C. (59° F.) to the boiling-point in eight and three-quarters minutes, with an expenditure of about 1 ounce of alcohol; low-grade alcohol of 75 or 80 per cent. evaporates less rapidly than stronger alcohol and produces equally good results.

For the combustion of coal-oil, stoves are now manufactured which are claimed to produce a smokeless and odorless flame; the heating capacity of these stoves is quite considerable, and is regulated by means of screws for raising and lowering the wick. Fig. 51 represents the Whitney patent hot-blast stove, in which the wick chamber is separate from the oil reservoir. Coal-oil stoves may be had with one, two, or three wicks, and require some attention, so that the wicks shall always be kept well trimmed and free from carbonaceous matter; to avoid a deposit of soot, the wick should never be allowed to touch the vessel to be heated.

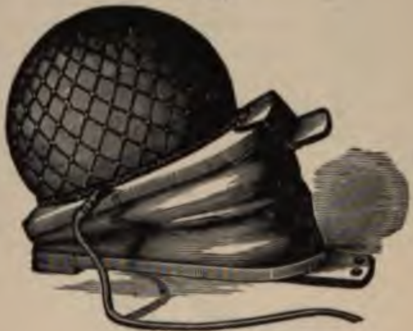
It is well known that the illuminating power of gas depends upon the incandescence of particles of unconsumed carbon, and that if these particles be brought to complete combustion by the appropriate use of air (atmospheric oxygen) the luminosity of the flame will be decreased, but its heating power will be intensified. A yellow carbonized flame, also known as oil flame, because resembling that produced by the combustion of oil, is never well adapted for heating purposes, besides depositing considerable soot or carbon on the bottom of vessels placed over it. In all modern gas-heating apparatus proper provision is made for mixing the illuminating-gas with such a proportion of air that, when the mixture is ignited, a purely blue flame will result, indicative of complete combustion; the flame of burning alcohol resembles such a flame. A large variety of gas burners and stoves is now offered, intended to furnish both high and low powers of heat. Of these, probably none has a wider range in heating capacity than the Fletcher low-temperature burner (Fig. 52), any degree of heat from a gentle current of warm air to bright red-heat being obtainable; it is manufactured by the Buffalo Dental Manufacturing Company, of Buffalo, N. Y. The burner consists of a ring of iron tubing, D, perforated on the upper side, and enclosed in a cylinder of cast iron, over which a diaphragm of wire gauze, A, is fastened; there is a space, B, between the lower end of the cylinder and the bottom of the apparatus, for the admission of air, and a tube, C, for the attachment of a pipe from a bellows when a blast is to be used for producing powerful heat. When a gentle heat is desired, the gas is

Fig. 52.



Fletcher low-temperature burner.

Fig. 53.

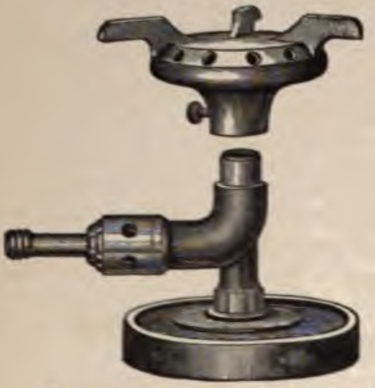


Foot-blower.

lighted through the opening B, thus heating the air as it flows upward and escapes through the gauze A. For a stronger heat the gas and air mixed are lighted above the wire gauze, and a steady, smokeless blue flame is thus obtained. As any rubber tubing attached to D is apt to become very hot, it should either be wrapped with a small wet cotton cloth, dipping in water, or, what is still better, about eight inches of gas-pipe should be permanently attached to D, to which the rubber supply-tube may be secured when wanted. Fig. 53 represents a convenient foot-blower for use with any gas furnace requiring a strong supply of air; the rubber disk is well protected by netting.

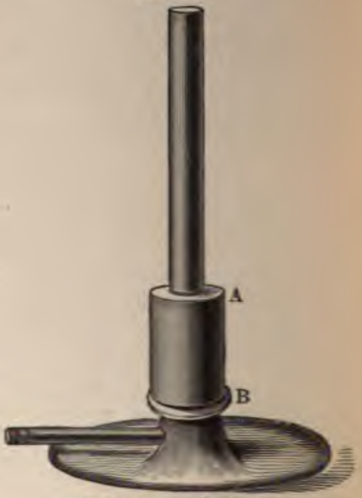
For small operations at the dispensing counter Bunsen burners are usually employed, which are so constructed that a small supply of gas is made to yield a strong heat by admixture with air, whereby perfect combustion is effected. One drawback to the majority of Bunsen burners in the market is the tendency to "light back"—that is, when the flame is reduced, it is apt to recede and ignite the gas at the pinhole orifice in the tube; the most effectual method of overcoming this difficulty is to contract the orifice of the tube and introduce a gauze diaphragm into it near the top, which, however, reduces the heating power of the flame. Among the large variety of Bunsen burners sold, a few have been found specially adapted to the needs of the pharmacist, and are here illustrated. Fig. 54 represents a low form of burner, 3 inches high, made in two sizes, with tubes of $\frac{5}{16}$ and $\frac{5}{8}$ inch diameter, respectively; with the aid of a contracted brass cap the flame can be turned down quite low without receding. When it is desired to distribute the flame the brass crown shown in the cut should be attached, after removal of the brass cap; the crown being provided with three supports, does away with the necessity for a tripod. The burner is made

Fig. 54.



Bunsen burner, low form with crown.

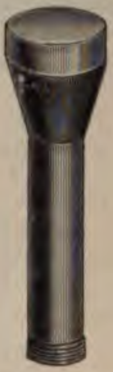
Fig. 55.



The Acme safety burner.

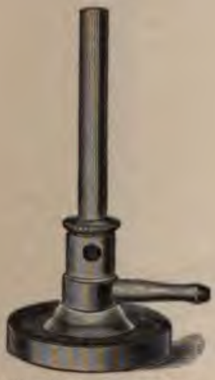
by Bullock & Crenshaw, of Philadelphia, and will be found very serviceable for all smaller operations. In Fig. 55 is shown the Acme burner, patented in 1891 by T. Boyce, of New York; this is probably the most satisfactory burner made for small operations at the dispensing counter, and can be used with coal or gasoline gas. Each burner is provided with two tubes, one of the regular Bunsen pattern, the other with a gauze safety-tip (Fig. 56), permitting the flame to be turned down as low as desired, and out without receding. The supply of gas is regulated by turning the tube at A until the desired size of flame is obtained; by turning the milled disk, B, up or down, it being threaded and moving upon the nipple, the air-supply is adjusted. The height of the burner is 5½ inches, including the base. The Finkner burner (Fig. 57) yields a very satisfactory flame, but is not adapted for very strong heat; it is so constructed that the supply of gas and admixture of air can be simultaneously regulated by turning the milled head. Fig. 58 represents a convenient adjustable burner; by turning the screw, which is accessible to the fingers while the burner is in use, the gas orifice can be so adjusted that any desired flame may be had. The air-supply is adjusted by turning the air-regulator up or down, it being threaded and moving upon the burner tube. The moving of the point up through the gas orifice, while reducing the gas quantity and size of the flame, does not reduce the gas pressure; the gauze safety-tip (Fig. 56) may also be attached to

Fig. 56.



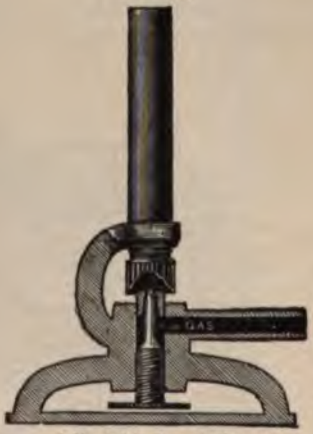
Gauze tip and tube for the Acme burner.

Fig. 57.



The Finkner burner.

Fig. 58.

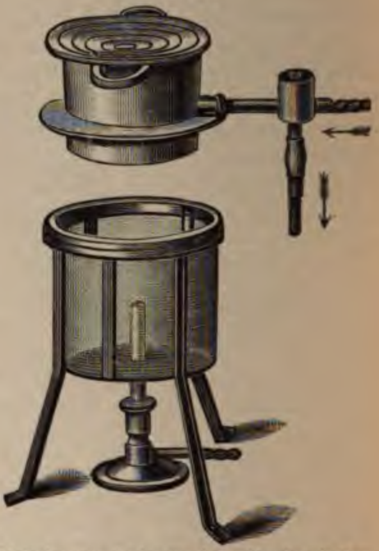


Adjustable Bunsen burner.

this burner when a very small flame is desired. For maintaining low temperatures, as in the testing of pepsin and similar operations, the double minim burner (Fig. 59) will be found useful.

For use with inflammable liquids the apparatus illustrated in Fig. 60 will be found serviceable, the burner being surrounded with safety gauze, which prevents the flame from communicating with the vapor on the outside, the principle being the same as in the Davy safety lamps.

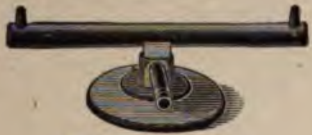
FIG. 60.



Safety burner, to be used for heating inflammable liquids.

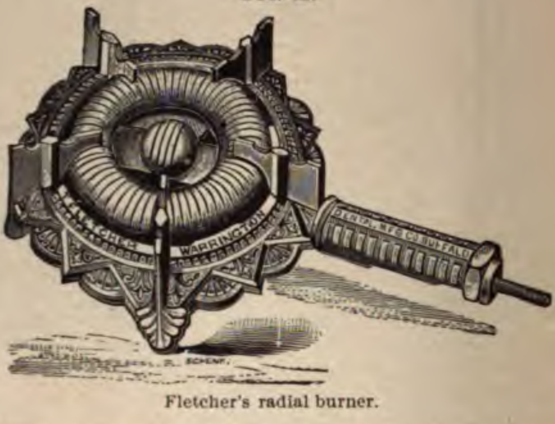
Fletcher's radial burner (Fig. 61) possesses some advantages over other heaters in containing no loose parts and in being made entirely of annealed cast-iron; it is practically indestructible; if choked with dirt, it is readily cleaned with a card or spatula. When in use, the flames are practically *solid* and show no tendency to run to a point in the centre; the consumption of gas amounts to from 12 to 18 cubic feet per hour,

FIG. 59.



Double minim burner.

FIG. 61.

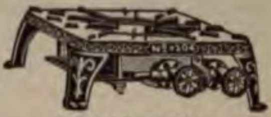


Fletcher's radial burner.

and the burner will accommodate vessels from 10 to 18 inches in diameter.

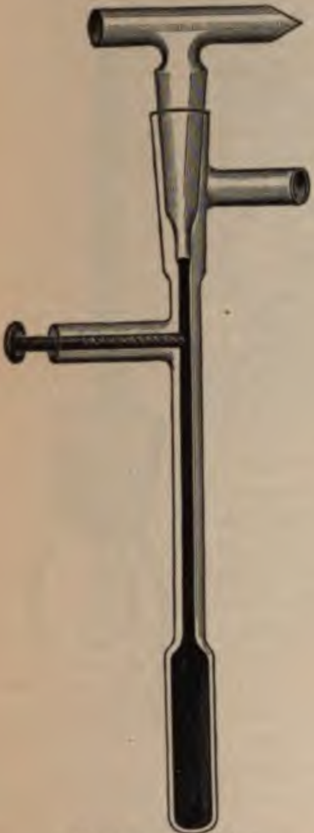
For larger operations the "Jewel" gas-stove, Fig. 62, manufactured by George M. Clark & Co., Chicago, will be found very serviceable. The cast-iron frame is 12 inches square and 5 inches high, thus standing very firm and capable of supporting large vessels. The gas is properly mixed with air before it enters the radial burner, where perfect combustion is effected, as shown by the pale-blue flame, which can be turned down very low without flickering. It consumes about 8 cubic feet of gas per hour, and is a most efficient heater.

Fig. 62.



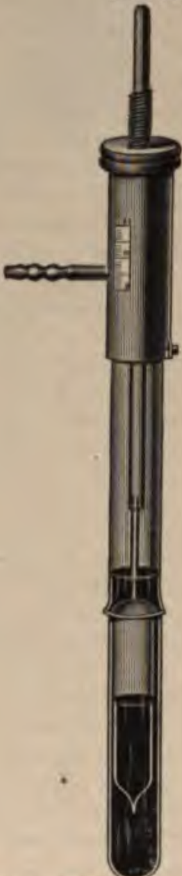
"Jewel" gas stove.

Fig. 63.



Reichert's thermostat

Fig. 64.

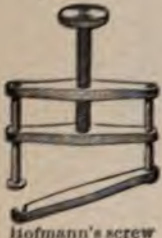


The Bunsen-Kemp gas regulator or thermostat.

For regulating the degree of heat within certain narrow limits, special appliances have been devised, known as thermostats, by means of which the supply of gas admitted to the burner is automatically controlled by expansion and contraction of mercury contained in glass cups or tubes kept in contact with the air or liquid the temperature of which it is desired to maintain at or near certain points. All gas supplied to the burner is made to pass through the thermostat, and the required temperature having been reached, the gauge is set by means of a screw, after which the supply of gas is controlled by the expansion of the mercury caused by an increase of heat. Figs. 63 and 64 show two thermostats frequently employed.

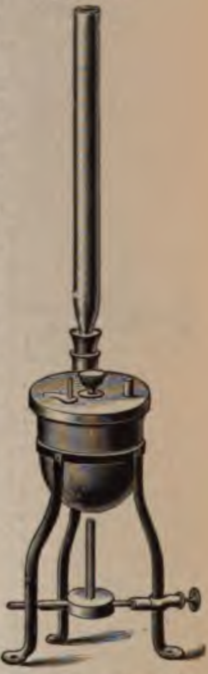
For ordinary operations, quite a fair regulation of temperature can be effected by means of the Hofmann screw compressor (see Fig. 65). The supply of gas being turned on full at the key and the screw having been slipped over the rubber tubing, the latter is compressed until the desired temperature is reached and maintained for some time. This plan is especially effective in connection with an air-bath when a temperature between 110° C. (230° F.) and 115° C. (239° F.) or higher may be desired. For definite lower temperatures between 60° C. (140° F.) and 100° C. (212° F.) the best method for maintaining constancy is by means of the Victor Meyer air-bath (see Fig. 66), which is so constructed that liquids of known boiling-points, below that of water, are heated in a jacket surrounding an inner compartment. A small quantity of the liquid, 6 or 8 Cc., is put into the outer jacket, and loss by evaporation prevented by means of a long glass tube inserted through the top of the jacket for the purpose of condensing the vapors and allowing the resulting liquid to flow back. These Meyer air-baths are much used in analytical laboratories, and may be employed for temperatures above 100° C. (212° F.) as well as below.

FIG. 65.



Hofmann's screw compressor.

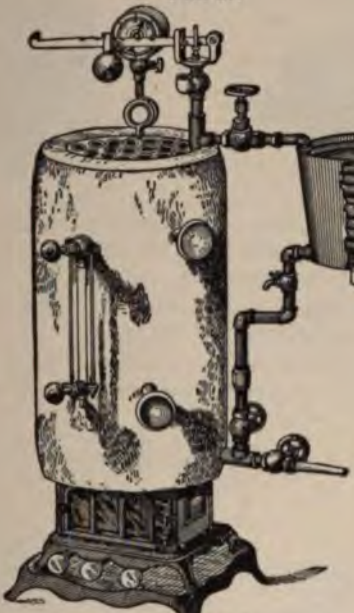
FIG. 66.



Victor Meyer air-bath.

The steam boiler, Fig. 67 designed by Prof. E. L. Patch, is a most convenient source of heat for the requirements of a small laboratory. The boiler, 22 inches high and 10 inches in diameter, is made of steel, contains 20 flues, and is covered with a thick layer of asbestos composition, to prevent loss of heat by radiation; it has a capacity of 7 gallons, and possesses one great advantage—that it can be heated by means of either a gas or a coal-oil stove. Being provided with a water-gauge, safety-valve, and manometer, the boiler is as complete as any of larger size, and steam can be carried from it to any point desired; it is usually filled from above at the safety-valve, but wherever water service is available an injector may be attached, so as to allow of filling while steam pressure is on. The coil of pipe in the conically shaped metal case on the side may be used for hot filtration, evaporation or drying purposes.

Fig. 67.



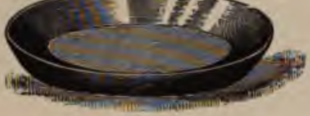
Patch's steam boiler.

It is well known that steam, when confined, is capable of absorbing large quantities of heat, and its temperature rises proportionally to the pressure exerted upon it; dense aqueous solutions, therefore, can readily be boiled by means of superheated steam.

For the proper control and distribution of heat, different devices are employed. When direct flame is to be applied to porcelain or glass vessels the interposition of wire-gauze or asbestos cloth will be found very desirable; for not only will the heat be supplied to a greater extent of surface by radiation, but at the same time it will be uniformly distributed, and thus insure more regular heating, which of itself is very important, considering the frail character of flasks and dishes.

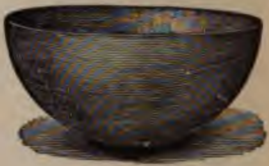
The sand-bath is employed for temperatures above that of boiling water, and is chiefly intended to furnish a continuous supply of high heat and to prevent sudden depression of temperature from extraneous causes; it is invaluable in the distillation of certain liquids (acids, etc.) from glass vessels, and may be either of deep or shallow form (see Figs. 68 and 69). The deep sand-bath consists of an iron pot or basin containing sufficient dry fine sand so that, if desired, the retort or flask may be entirely surrounded by the same. The best shallow sand-baths are made of Russian sheet-iron, and are well adapted for heating flasks and beakers, which require only sufficient sand to form a good bed of support, since an excessive amount would involve a waste of heat.

FIG. 68.



Sand-bath, shallow form.

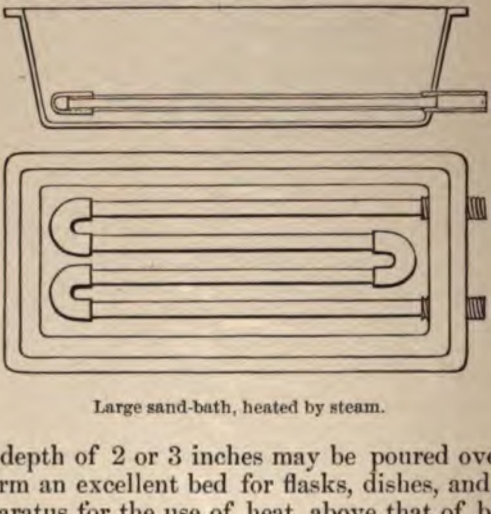
FIG. 69.



Sand-bath, deep form.

For use in a laboratory where steam is available a permanent sand-bath may be provided as shown in Fig. 70. It is constructed from an ordinary galvanized-iron sink and large gas-pipe, about $\frac{3}{4}$ to 1 inch in diameter, arranged horizontally as shown in the figure.

FIG. 70.



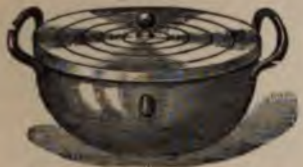
Large sand-bath, heated by steam.

Sand to the depth of 2 or 3 inches may be poured over the pipes, which will form an excellent bed for flasks, dishes, and beakers.

Other apparatus for the use of heat above that of boiling water, yet avoiding contact with flame direct, are oil-baths, saline-solution baths, glycerin-baths, or paraffin-baths: these are constructed like water-baths, and readily furnish temperatures ranging from 100° to 300° C. (212° to 572° F.).

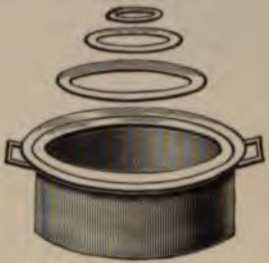
For all operations requiring a degree of heat below that of boiling water water-baths will be found indispensable; they may be made with either a round or a flat bottom, as shown in Figs. 71 and 72, and provided with a set of concentric rings to adapt them for use with dishes or flasks of various sizes. Water-baths made of extra heavy tin will last a long time (provided they be dried properly after use), and do not cost much, while copper is far more expensive, but, on the other hand, resists the action of heat and water better than tinned iron. As long as the vapor of boiling water is allowed to escape freely no amount of heat applied to the vessel can possibly increase the temperature of the water above that of boiling, and, as some heat-power is lost during transmission from the water-bath to the vessel resting upon it, the liquid contained in such vessel will always be found a few degrees lower in temperature than the

FIG. 71.



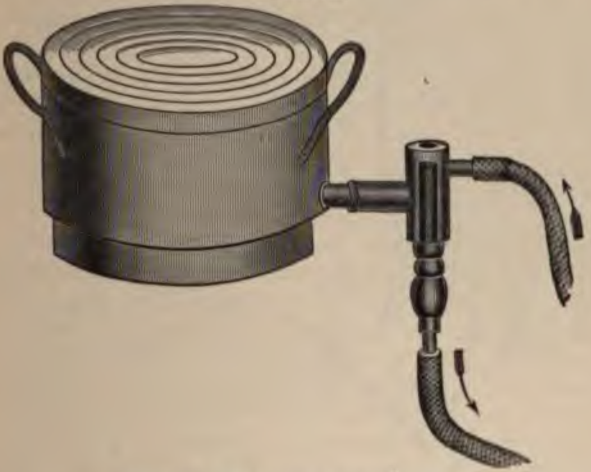
Round-bottom water-bath.

FIG. 72.



Flat-bottom water-bath.

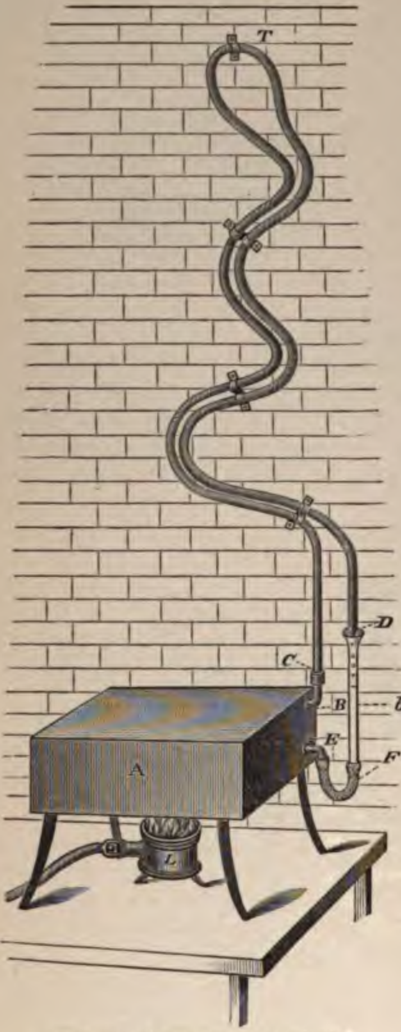
FIG. 73.



Water-bath with constant-level attachment.

water in the bath; under no circumstances can aqueous liquids be made to boil in dishes placed in water-baths. The name vapor-bath is in the majority of cases more appropriate than water-bath, since the vessel heated by it does not, as a rule, come in contact with the water for any length of time, but derives its heat from the vapor or steam rising from the water and not confined by pressure.

FIG. 74.



Davenport's constant water-bath.

To avoid frequent refilling and consequent interruption in long-continued operations, water-baths are often provided with a constant-supply attachment, as shown in Fig. 73, which also serves to keep the water at a constant level in the bath. The best contrivance for a constant water-bath is that suggested by Dr. B. F. Davenport, of Boston, and shown in Fig. 74. It consists of a copper box, *A*, 10 or 15 inches square, the top being a brass plate $\frac{1}{8}$ inch thick, to enable it to bear considerable weight without yielding. From the point *B* projects a $\frac{1}{2}$-inch brass tube, *BC*, which turns up at a right angle. At *E* is a stopcock which is connected by a thick rubber tube with the glass tube *DF*, the latter being fastened to the adjoining wall. Connected with *C* by a rubber tube-joint is a $\frac{1}{2}$-inch block-tin tube of 20 feet length, which extends up the wall, to which it is fastened for 10 feet to the point *T*, whence it returns and ends just over the top of the glass tube at *D*. The bath is filled with water (preferably distilled) to just the level *B*..*b*. The steam generated by the constant boiling is condensed in the tube *CTD*, either before or after reaching the top *T*, and returns to the bath at *C* or at *D*, where it drops into the glass water-gauge *DF*.

Having once been filled, the water need not be replenished for years, and there being no outlet for the steam except into the condensing tube, the air surrounding the water-bath will be kept constantly dry—a very desirable point in the evaporation of liquids. If the water-bath is desired for use at fixed temperatures, a thermometer may be introduced through a cork fitted to a tube inserted in the cover of the bath.

The boiling-point of a liquid is that at which the elasticity of its vapor overcomes the pressure of the surrounding atmosphere; or, in other words, beyond which it cannot continue as a liquid without increased pressure. Normal atmospheric pressure, 15 pounds to the square inch, which is equal to the pressure of a column of mercury 760 Mm. (29.87 + inches) in height, is always assumed when referring to the boiling-point of a liquid, for any modification of the former will change the latter; thus water, which ordinarily boils at 100° C. (212° F.), has been known to boil at 84° C. (183.2° F.) on Mont Blanc, and even at 35° C. (95° F.) in a vacuum apparatus; while under greatly increased pressure, as in Papin's digester, it has been heated to 160° C. (320° F.) without boiling. There exists also a great variability in the boiling-points of different liquids under normal conditions; for, while official ether boils at about 35.5° C. (96° F.), chloroform requires a temperature of 60.5° C. (140.9° F.), alcohol 78° C. (172.4° F.), glycerin 165° C. (329° F.), mercury about 357° C. (674.6° F.).

The simplest method for determining the boiling-point of a liquid is to introduce some of it into a flask provided with a lateral tube in the neck and a thermometer passing through the cork, as shown in Fig. 75, or into an ordinary Florence flask provided with a double perforated cork, through one orifice of which a thermometer is inserted and through the other a bent glass tube, as represented in Fig. 76. If inflammable or noxious vapors are likely to be evolved, the tube from either flask may be connected with a condenser. It is important that the thermometer should not be immersed in the liquid, but only introduced into the flask so far that the bulb may be enveloped by the vapor of the boiling liquid, as shown in the illustrations. Heat should be carefully applied and gradually increased until the liquid boils actively, at which time the boiling-point will be indicated by the height of the mercurial column in the thermometer. In the case of very accurate determinations, it may be necessary to make corrections for increased or decreased atmospheric pressure; and according to Kopp, the correction amounts to 1° C. (1.8° F.) for every 27 millimeters above or below the normal height of the barometer column of mercury. In order to avoid errors which might arise from the cooling of the long mercurial column outside of the flask, specially constructed thermometers, known as Zincke's thermometers (see p. 99) are usually employed for temperatures above 100° C. (212° F.).

Fusible substances when gradually heated to their melting-point do not all behave in the same manner; as a general rule, crystallizable bodies become brittle just before melting, while non-crystallizable substances assume a plastic condition. When fusion commences they combine, as it were, with heat in an intimate manner—that is, they occlude heat, so that the further addition of heat does not cause any rise in temperature until all of the substance has become liquefied. The heat thus disappearing is called the latent heat of fluidity, because it is used to change the solid form of a body into the liquid form without any change in the temperature of the body; thus if crushed ice be heated, the temperature will not vary from 0° C. (32° F.) while the ice is melting, and when completely changed to water the temperature of the water will also be 0° C. (32° F.) provided the application of heat be not continued beyond fusion. The amount of heat necessary to produce complete fusion varies with different substances and at different temperatures; thus in the case of ice at 0° C. (32° F.), it has been found equivalent to the amount of heat necessary to raise the temperature of an equal weight of water from 0° C. (32° F.) to 79.25° C. (174.65° F.). This was determined as follows: Two vessels containing respectively equal weights of ice and water at 0° C. (32° F.), and each provided with a thermometer, were heated in a bath of water; at the moment when the ice had completely melted the temperature was indicated as still at 0° C. (32°

Fig. 75.

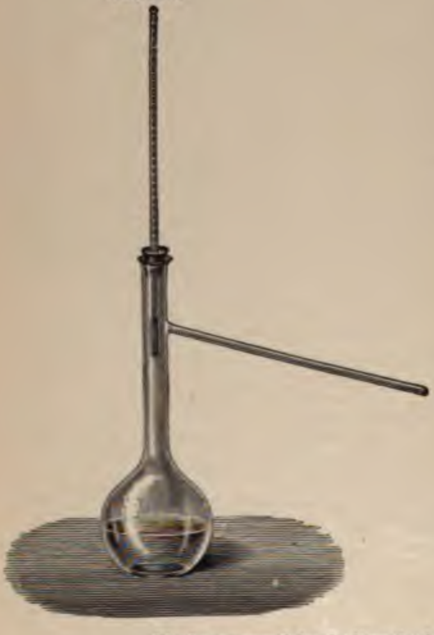
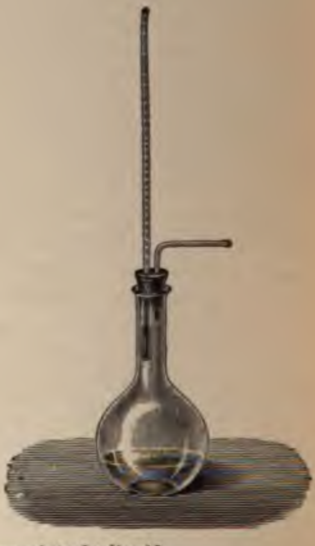


Fig. 76.



Flasks arranged for finding the boiling-point of a liquid.

F.), while the temperature of the water in the other vessel had risen from 0° C. (32° F.) to 79.25° C. (174.65° F.). If 1 pound of ice at 0° C. (32° F.) and 1 pound of water at 100° C. (212° F.) be mixed so as to avoid loss by evaporation, the result when all the ice has melted will be 2 pounds of water at 10.4° C. (50.7° F.); whereas if 1 pound of water at 0° C. (32° F.) be mixed with 1 pound of water at 100° C. (212° F.), the result will be 2 pounds of water at 50° C. (122° F.). In the first case, 79.25 C. (142.65 F.) degrees of heat were withdrawn from the boiling water to melt the ice at 0° C. (32°F.) into water at 0° C. (32° F.); but in the second case this was not necessary, and the mixture assumed the mean temperature of the two liquids. Physicists express this latent heat of fusion in terms of calories, the word calorie being used to designate the amount of heat necessary to raise the temperature of 1 gramme of water from 0° C. (32° F.) to 1° C. (33.8° F.). The latent heat of fluidity of water being known as 79.25° C., a simple rule can be formulated for ascertaining the amount of ice necessary to reduce any given weight of water from a stated temperature to a stated lower temperature, as follows:

Add the desired temperature to 79.25 *degrees Centigrade and divide the sum into the difference between the stated temperature of the water and the desired temperature;* the quotient will be the required proportion of ice as compared with the given weight of water.

Example: How much ice is required to cool 1000 Gm. of water from 100° C. to 25° C.?

```
 79.25        100.0        104.25)75.000(0.7194
 25.00         25.0               72975
104.25         75.0                20250
                                   10425
                                    98250
                                    93825
                                     44250
                                     41700
```

Answer: 0.7194 of 1000, or 719.4 Gm.

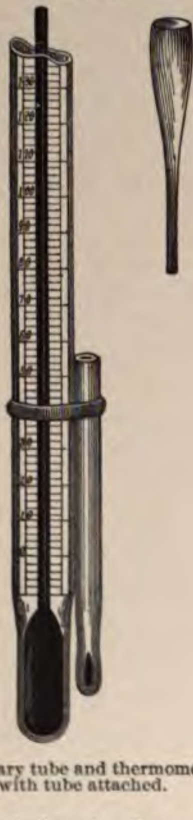
Proof: The ice needs 25° C. in addition to the 79.25° C. required for melting it, and the water loses 75° C. by the reduction of its temperature to 25° C.; as the gain and loss must balance each other, it will require $\frac{75}{104.25}$ of 1000 Gm. of ice, or 791.4 Gm.

The law regarding latent heat of fluidity has a practical bearing upon the fusion of various substances liable to be injured by exposure to a temperature a little above their melting-points; thus, a pan of ointment or plaster may be kept over a direct fire without danger of injury *as long as a portion of the contents remains unmelted,* as the increased amount of heat is utilized in the change of the state of aggregation.

The melting-points of solids are as variable as are the boiling-points of liquids; thus, while ice melts at 0° C. (32° F.) and lard at 39° C. (102.2° F.), sulphur requires a temperature of 115° C. (239° F.) and pure morphine a temperature of 255° C. (491° F.).

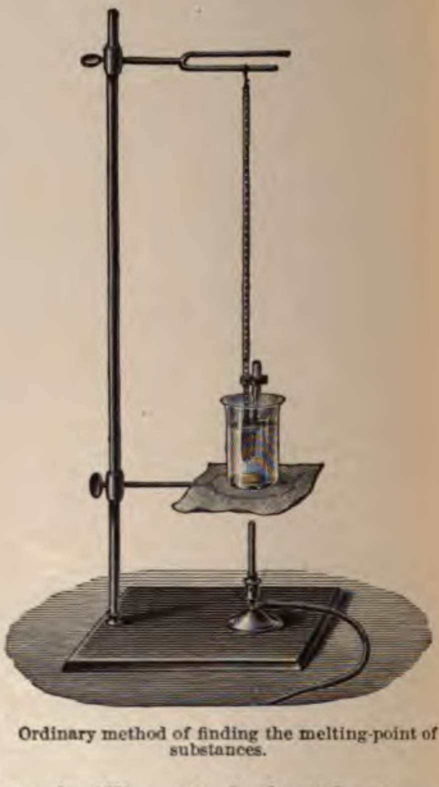
The determination of the melting-point of a substance frequently leads to its identification, and is a most valuable adjunct in the examination of its quality. Some care is requisite in determining the melting-point, so as to insure accurate results. The best plan is to put a little of the substance to be examined into a small capillary tube (Fig. 77), and after cutting off the enlarged portion, which is intended only for convenience in filling, attach the tube to an accurate thermometer by means of a rubber band in such a manner that the tube lies close against the thermometer and the substance is on a line with the bulb, as shown in Fig. 77. The thermometer thus arranged may be suspended in a beaker containing water, sulphuric acid, or paraffin, as shown in Fig. 78. The liquid is gradually heated and the temperature accurately noted when the substance in the capillary tube melts.

FIG. 77.



Capillary tube and thermometer with tube attached.

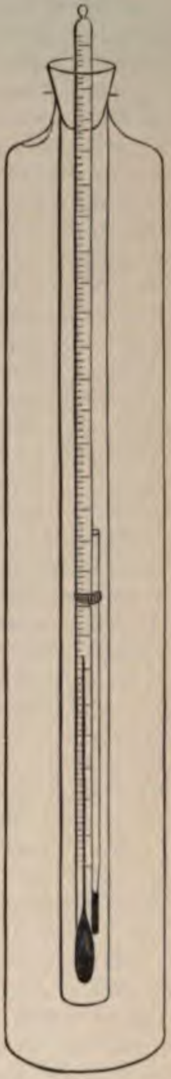
FIG. 78.



Ordinary method of finding the melting-point of substances.

'he simple apparatus shown in Fig. 79 is intended to insure ter uniformity in heating the mercurial column of the thermom- by suspending the latter in a tube enclosed in another filled about ¾ with sulphuric acid. temperature of the air surrounding the ther- ieter in the inner tube is kept uniform by ilation of the acid fluid in the outer tube n heat is applied.

FIG. 79.



Improved apparatus for the determination of melting-points.

'he term *temperature* is used to designate *in- ty* but not *quantity* of heat, which is measured thermometer, an instrument consisting of a ow capillary tube of uniform bore, hermeti- sealed at the upper end and terminating w in a bulb of glass. The bulb and a por- of the tube are filled with mercury (in some s with colored alcohol or toluene), and the le is provided with a graduated scale for suring the rise and fall of the liquid within tube; mercury is preferred for all tempera- s not below —40° C. (at which point it es), on account of its non-adhesion to the of the glass tube and consequent convex ice, and its great sensitiveness to even the itest change in temperature. Absolute alco- although admirably adapted for very low peratures, cannot be used for measuring heat isity above 78.3° C. (172.9° F.), its boiling- t. The space above the liquid in the tube is ived of air, so as to insure the ready and orm rise of the liquid when expanded by .

ls all glass vessels continue to contract for time after they have been made, absolutely ect measurement of temperature can only be ined if the error of the thermometer is known then applied for correction of the reading. ical thermometers, used by physicians for ng the temperature of fever patients, should riably be supplied with a certificate showing error, as this may in some cases amount to ly ½ degree. Since 1901 the U. S. Govern- t has had in operation a Bureau of Standards he Department of Commerce and Labor at hington, D. C., where clinical thermometers be examined and certificated. The following e method pursued: After careful examination defects of construction, the thermometer is compared with the lard thermometers of the bureau at the four test-points 96°, , 104°, and 108°, two independent comparisons being made at each point. If the two tests at any point differ by more than 0.15° F., or if the mean of the two tests give a correction in excess of 0.3 degree, the thermometer is rejected. Moreover, errors in the intervals between test-points must not exceed 0.3° F.; for example, if the correction at 96° is 0.3°, and at 100°, 0.1°, the error in the interval would be 0.4°, and the thermometer would be rejected. Careful examination of the index is also made, and if upon trial, by means of a special whirling device, the index fails to return to its original position, showing that it is too difficult to shake down, the thermometer is rejected. The results of these examinations, in tabulated form, are furnished the applicant who submits the thermometers, and thus the exact error of each thermometer becomes known. Pharmacists who supply physicians with clinical thermometers should demand that each instrument be supplied with a government certificate. All clinical thermometers should be "seasoned" or "aged" for a year two before they are examined, so that any error found may remain constant.

Experiments made by the Bureau of Standards have shown that where ordinary domestic glass is used in making all parts of the thermometer, the average increase in the reading at the end of two months is 0.3 of a degree, and at the end of fourteen months 0.68 of a degree. If French hard glass or Jena normal glass is used, the average change in the reading at the end of two months has been found to be only 0.06 of a degree, and at the end of fourteen months 0.11 of a degree. Some manufacturers of thermometers now make the bulb of hard glass (because the contraction of this part of the instrument causes the greatest error) and the stem of softer glass.

Since 1893 thermometers of great accuracy, intended for very high temperatures, up to 550° C. (1022° F.), have been made in Germany, of special glass, known as "Jena resistance glass," which is very hard and non-contractile. In order to prevent boiling of the mercury, which ordinarily occurs at about 357° C. (674.6° F.), the capillary tube is expanded at the upper end and filled above the mercurial column with compressed dry carbon dioxide. Thermometers of still higher range have been manufactured in which the indicator consists of an alloy of sodium and potassium, instead of mercury, and which may be used for temperatures as high as 650° C. (1202° F.). The alloy is also enclosed in "resistance glass," and the space above the alloy is filled with nitrogen at such pressure that when the bulb becomes red-hot the pressure inside is equal to that of the atmosphere. The glass of the bulb is attacked by the alloy and stained brown; but this occurs at the time of filling, and the coating then formed upon the surface of the glass protects it from further action.

For registering still higher temperatures, instruments known as pyrometers are employed, which are, however, not very trustworthy; they are of two kinds, Wedgewood's pyrometer, based on the contraction of clay, and Brogniart's pyrometer, based on the expansion of metals. When it is desired to note the highest or lowest temperature reached during any fixed time, maximum and minimum thermometers, so constructed that a small metallic or glass indicator is carried to the highest or lowest point reached by the mercury or alcohol, and left at that point when the volume again changes, are used.

Three different thermometric registers, known as the Fahrenheit, Réaumur, and centigrade scales, are in use. The centigrade scale is used in France, and is now universally employed for scientific purposes, while the Fahrenheit scale is in common use in this country and Great Britain, and the Réaumur scale is ordinarily used in Germany. The graduations of all three scales are arbitrary, yet based upon careful observations of their respective authors. Fahrenheit, a German, who, while living in Holland, invented the mercurial thermometer in 1714, divided his scale ranging from 0° to 96°, according to three fixed points. The first point, marked zero, was found by noting the level to which the mercury fell in the thermometer when the instrument was immersed in a mixture of water, ice, and ammonium chloride (or sea salt), supposed to be the greatest cold attainable. The proportions used by Fahrenheit for this experiment are unknown, and have not been duplicated since. The second point was obtained by placing the thermometer in a mixture of ice and water or in melting ice, and indicated the level to which the mercury fell when thus immersed. This point was called the beginning of freezing, and corresponded with the 32d division of Fahrenheit's scale. The third point was that reached by the mercury upon introducing the thermometer into the mouth of a healthy man, and holding it there for a few minutes. The scale was afterward extended to 600°. The origin of the degree 212 for boiling water was probably accidental, since Fahrenheit does not appear to have used the boiling-point of water as a fixed point, and had no intention of dividing the interval between his zero and the boiling-point of water into 212 parts. It is probable that the 212th division on Fahrenheit's scale, after extension, happened to coincide with the level of the mercury in the thermometer at the boiling-point of water. The present Fahrenheit scale is evidently not identical with the original, but the result of improved methods; for while the temperature of the human body was marked at 96° on the original scale, it stands at 98° on the scale now in use. Réaumur, a Frenchman, about 1730, found that 1000 volumes of a mixture of alcohol with $\frac{1}{5}$ water expanded to 1080 volumes between the freezing- and boiling-points of water, and he marked these extremes as 0 and 80 respectively, dividing the intervening space into 80 equal parts. Celsius, a Swede, in 1742, proposed a scale with 0 at the boiling-point of water and 100 at the temperature of melting ice. This scale was modified and inverted by Christin, of France, and Strömer, of Sweden, independently, in 1743, and thus the present centigrade scale was introduced. It has also been claimed that the centesimal division of the thermometric scale between the freezing- and boiling-points of water was first made by Linné, the famous Swedish botanist, for use in greenhouses.

since 80 degrees on the Réaumur scale equal 180 degrees on the Fahrenheit scale, each degree of the former must correspond to 2.25 degrees of the latter. Each Réaumur degree is equal to 1.25 centigrade degrees. The following rules for the conversion of thermometric values are useful.

To convert centigrade into Fahrenheit: *Multiply by* 1.8 *and add* 32; for any number of degrees above or below the freezing-point on the centigrade scale when multiplied by 1.8 yields the corresponding number of degrees above or below the freezing-point on the Fahrenheit scale.

To convert Fahrenheit into centigrade: *Subtract* 32 *and divide by* 1.8; for any number of degrees above or below the freezing-point on the Fahrenheit scale when divided by 1.8 yields the corresponding number of degrees above or below the freezing-point on the centigrade scale.

To convert Réaumur into Fahrenheit, or Fahrenheit into Réaumur, *substitute* 2.25 *for* 1.8 *in the preceding rules.*

To convert centigrade into Réaumur, *divide by* 1.25; and to convert Réaumur into centigrade, *multiply by* 1.25.

Examples: Convert 25° C. into F.; 25 × 1.8 = 45, and 45 + 32 = 77. Answer, 77° F.
Convert − 15° C. into F.; − 15 × 1.8 = − 27, and − 27 + 32 = 5. Answer, 5° F.
Convert − 40° C. into F.; − 40 × 1.8 = − 72, and − 72 + 32 = − 40. Answer, − 40° F.
Convert 60° F. into C.; 60 − 32 = 28, and 28 ÷ 1.8 = 15.55 +. Answer, 15.55 + ° C.
Convert 18° F. into C.; 18 − 32 = − 14, and − 14 + 1.8 = − 7.77 +. Answer, − 7.77 + ° C.
Convert − 12.5° F. into C.: − 12.5 − 32 = − 44.5, and − 44.5 + 1.8 = − 24.72+. Answer, —24.72 + ° C.
Convert 30° R. into F.; 30 × 2.25 = 67.5, and 67.5 + 32 = 99.5. Answer, 99.5° F.
Convert − 5° R. into F.; − 5 × 2.25 = − 11.25, and − 11.25 + 32 = 20.75. Answer, 20.75° F.
Convert 50° F. into R.; 50 − 32 = 18, and 18 + 2.25 = 8. Answer, 8° R.
Convert 4° F. into R.; 4 − 32 = − 28, and − 28 + 2.25 = − 12.4. Answer, − 12.4° R.
Convert 60° C. into R.; 60 + 1.25 = 48. Answer, 48° R.
Convert − 8° C. into R.; − 8 + 1.25 = − 6.4. Answer, − 6.4° R.
Convert 28° R. into C.; 28 × 1.25 = 35. Answer, 35° C.
Convert − 7.5° R. into C.; − 7.5 × 1.25 = − 9.37 +. Answer, − 9.37 + ° C.

In order to avoid the use of the ordinary long thermometer for temperatures above 100° C., which might frequently prove annoying and give rise to inaccuracies in scientific work, special short thermometers have been devised, so constructed that the graduations of the scale begin a little below the boiling-point of water (see Fig. 81). These instruments, known as Zincke's thermometers, are from 4 to 6 inches in length, very accurately made, and are admirably adapted for testing the melting- or boiling-point of substances at temperatures above 100° C.

In pharmacy arbitrary terms are frequently employed to indicate temperatures suitable for certain operations; thus the term *gentle heat* indicates a temperature between 32° and 38° C. (90°–100° F.), and the term *moderate heat* is employed when a temperature between 45° and 50° C. (113°–122° F.) is to be used and not exceeded.

CHAPTER V.

COLLECTION AND PRESERVATION OF CRUDE DRUGS.

ALTHOUGH the collection and preparation of vegetable drugs are not in the hands of the pharmacist, but are carried on, often in a small way, by special drug-gatherers and -collectors, it is thought fit to refer to the subject here.

The various parts of plants used in medicine cannot be gathered indifferently at all seasons of the year, since the peculiar juices of the plant in which its activity resides are more abundant in some parts than others at certain periods of the plant's growth. Roots of *annual* plants should be gathered immediately before the time of flowering; those of *biennials*, either late in the fall of the first year or early in the spring of the second year, after the first appearance of the plant above ground; perennial roots should not be gathered until after two or three years' growth, and in some cases even four or five years are allowed for full maturity. Fleshy roots should be sliced, either transversely or longitudinally, previous to drying, in order to expose a larger surface to the air; while smaller and fibrous roots do not require this treatment. When artificial heat is used in drying roots, a temperature of 50° to 55° C. (about 122° to 131° F.) is sufficient, except in the case of a few succulent roots, where the temperature may be raised to 65.5° C. (150° F.).

Barks of trees should be gathered in the spring, but those of shrubs in the autumn, for at these seasons they are most readily separated from the wood. Only the inner bark being employed, the outer epidermis should be removed.

Leaves begin to lose their activity after the flowers appear, for the juices of the plant then go toward nourishing the latter; they should therefore be collected when fully developed, before they begin to wither. Leaves of biennials should be collected during the second season.

Herbs are generally understood to mean the whole plant, although the root is frequently rejected; they should be gathered when in flower. If the flowers are not to be used with the stem, the latter should be collected before the flowers appear, but after foliation.

Flowers are preferably gathered before they are perfectly developed (expanded), since odor and color are then more pronounced; the red or French rose offers a striking example. They should be collected in the morning, after the dew has disappeared, and be dried, without artificial heat, in the shade.

Fruits should be gathered before they are quite ripe; but seeds, the least perishable of vegetable productions, must be perfectly ripe, and require very little drying.

Crude vegetable drugs are rarely deprived of all their inherent moisture by the drug-gatherers, and invariably reabsorb moisture when exposed to a damp atmosphere; before such drugs can be mechanically subdivided they frequently require a further drying by artificial heat, which is effected by spreading the material loosely on perforated shelves in ventilated apartments heated by steam. While drugs containing volatile constituents, such as buchu, valerian, myrrh, spices, etc., demand a moderate heat, others again can be strongly heated until they become brittle, as, for instance, squill; a temperature kept at or below 45° C. (113° F.) will not prove injurious in any case.

The amount of moisture present in freshly gathered botanical drugs varies considerably, ranging from 15 or 20 per cent. in barks and wood to as much as 80 per cent. or more in some roots and leaves, and the object of thorough drying is partly to reduce the bulk, but chiefly to preserve the drug for future use; for if vegetable drugs be packed away in a moist condition they soon begin to mould, or become heated, and undergo rapid deterioration. The following table by Tschirch shows the average loss in weight by drying, of a number of well-known drugs:

Name of Drug.	Loss.	Name of Drug.	Loss.
Althæa,	75 per cent.	Glycyrrhiza,	67 per cent.
Arnica flowers,	80 "	Mezereum,	50 "
Belladonna leaves,	82 "	Peppermint,	80 "
Belladonna root,	62 "	Squill,	75 "
Calamus,	75 "	Stramonium leaves,	55 "
Colchicum root,	66 "	Taraxacum,	78 "
Digitalis,	80 "	Valerian,	75 "

The loss in weight resulting from thorough drying of drugs is in many cases more than compensated for by the increase in value of the dried article, as in opium and other alkaloidal or resinous drugs. If opium containing 10 per cent. of morphine and 25 per cent. of moisture be dried perfectly, the loss in weight will amount to one-fourth, but the relative proportion of active principle is increased one-third; jalap tubers containing 8 per cent. of resin and 34 per cent. of moisture will lose upon drying about one-third of their weight, but the proportion of resin present is increased 50 per cent. Dried botanical drugs are best preserved in cool, dry rooms in containers which shall exclude sunlight, but permit of free circulation of air; odorous drugs should always be kept separate in order to avoid contamination of others; for instance, a bale of buchu, valerian, or sassafras should never be stored by the side of senna leaves, elm-bark, or flaxseed.

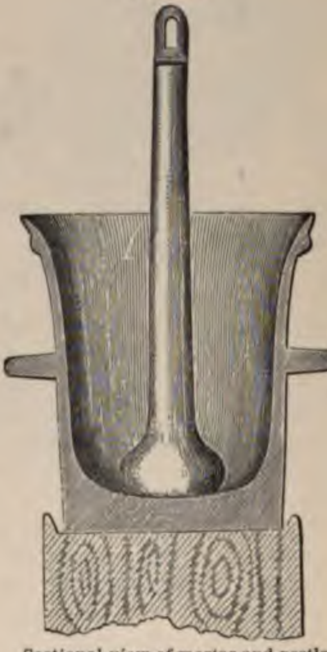
As crude drugs reach the pharmacist they are frequently not in a condition to be offered for sale, or to be used in the preparation of medicines, on account of impurities present, and the process of garbling is a very necessary operation. The object of garbling, or picking, is to remove, besides impurities and adulterations, decayed and deteriorated portions of the drug, which not only mar the appearance but are apt to contaminate the still healthy portion, and soon render the whole worthless. Senna leaves are generally accompanied by a considerable proportion of stems, broken capsules, and dust, not to speak of the fraudulent admixtures of stones, shells, etc., made by the gatherer or exporter for the purpose of increasing the weight; as much as 15 per cent. of impurities has been taken from what was bought as prime senna. Juniper berries are never free from unripe and decayed fruit, dirt, and worm-eaten portions, which should be carefully removed. Fibrous roots, as spigelia, wild ginger, serpentaria, and the like, require to be freed from adhering dirt and other roots that grow side by side with them, and have become mixed through careless gathering. Although some drugs are found in much better condition than others, there is none which may not be improved in appearance, even if it be only to have the fine dust and dirt removed, as in the case of sassafras, wild cherry, crushed oak-bark, etc.; lycopodium, fennel, flaxseed, and similar drugs should be well shaken in a suitable sieve, to remove foreign matter, before putting them away in containers: and the careful pharmacist will find that this little extra labor is readily appreciated by his patrons, who are apt to judge a man largely by the appearance of his wares. Even vegetable powders, such as ipecacuanha, nutgall, and others of similar character, must be passed through a fine sieve, preferably bolting-cloth, to remove coarse particles which unfit them for dispensing purposes, and which have in some instances been found to amount to as much as 25 per cent. of the total weight of the powdered drug.

CHAPTER VI.

MECHANICAL SUBDIVISION OF DRUGS.

BEFORE employing vegetable drugs in the various pharmaceutical preparations, it often becomes necessary to reduce them to a state of comminution, or of powder, more or less coarse or fine as the nature of the drug and the desired preparation may demand. By simple contusion is generally understood a rather coarse division, brought about by crushing or bruising in suitable apparatus preparatory to finer reduction; for small operations an iron or brass mortar of bell or urn shape is employed, which should be deep and with a broad inner base, as shown in Fig. 82, the pestle being of such length and weight as will enable the operator to exercise considerable force if necessary. In contusing substances only such a quantity should be placed in the mortar at one time as to cover the bottom for the depth of an inch or two; and to avoid loss or unpleasant results from the escape of dust or particles of drug, a cover, provided with a hole through which the pestle passes, should be used. In place of the mortar and pestle a cutting knife can frequently be used with advantage. The Champion knife No. 2, Fig. 83, made by the Enterprise Manufacturing Co., of Philadelphia, is well adapted for the coarse division of roots, barks, and herbs, as it combines a drawing motion with pressure while cutting the material. When operating on large quantities, steam power is necessary, and the best apparatus for the purpose is that known as Mead's disintegrator (see Figs. 84, 85, and 86). The grinding is done in this mill by hardened steel beaters securely riveted on both sides of a steel disk. These beaters revolve on the feeding side of the mill between corrugated rings. The beaters catch the material as it enters the mill and beat it against the corrugates until it is sufficiently fine to pass between

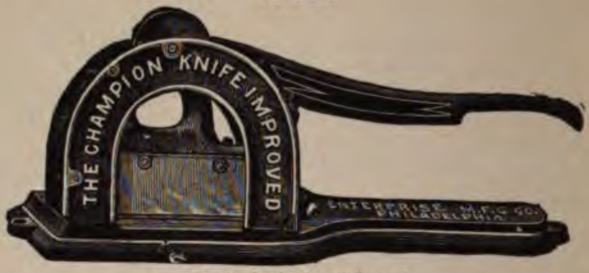
FIG. 82.



Sectional view of mortar and pestle for contusion.

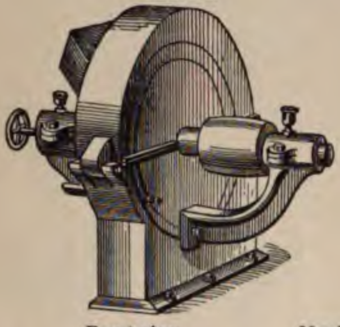
the disk and the face of the ring; as soon as it passes here it is on the discharge side of the mill, and all that is sufficiently fine is immediately driven out by the beaters on the back of the disk. What is not sufficiently fine to discharge is caught by these back beaters and beaten against the screens until fine enough to pass through. The screens are made of square steel, and present a grinding surface to the beaters and a discharging surface between each bar; they are 2 inches in width and extend around three-fourths of the diameter of the mill, thus giving a large discharging surface without diminishing the grinding surface. The material as it is ground falls into the box or room below. The most effective work is achieved with the disintegrator running at high speed, 3000 revolutions per minute; under such conditions 600 pounds of wild-cherry bark can be finely crushed in an hour.

Fig. 83.



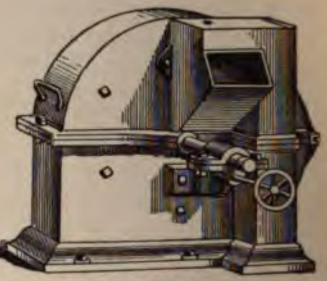
Cutter for herbs and roots.

Fig. 84.



Front view.

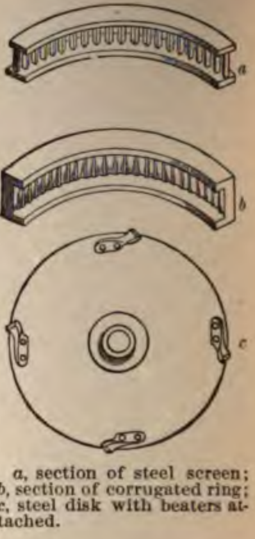
Fig. 85.



Side view.

Mead's disintegrator.

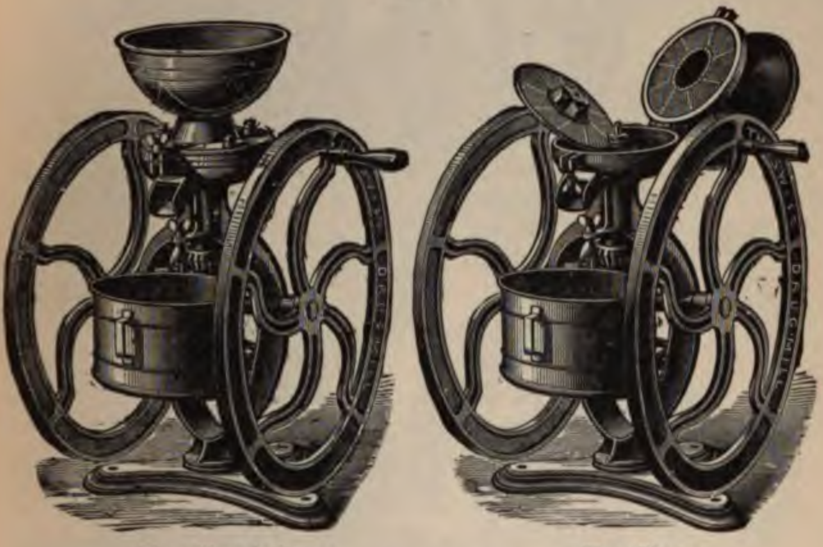
Fig. 86.



a, section of steel screen; *b*, section of corrugated ring; *c*, steel disk with beaters attached.

The production of very fine powders of drugs has long since passed into the hands of the drug-miller, and even the coarser powders intended for percolation are to-day prepared by only a small number of pharmacists. For the latter purpose the drug mills shown in Figs. 87 and 88 will be found very desirable. In the New *B* Swift mill the grinding is done between plates placed horizontally, while in the Enterprise mill they are placed vertically. The grinding surfaces of both mills consist of circular chilled-iron castings studded with concentric rows of sharp teeth, those of one plate fitting between those of the other. The teeth decrease in size toward the centre, and the fineness of the powder is regulated by a pair of screws, by means of which the plates are made to approximate each other. One of the plates is stationary while the other revolves.

FIG. 87.

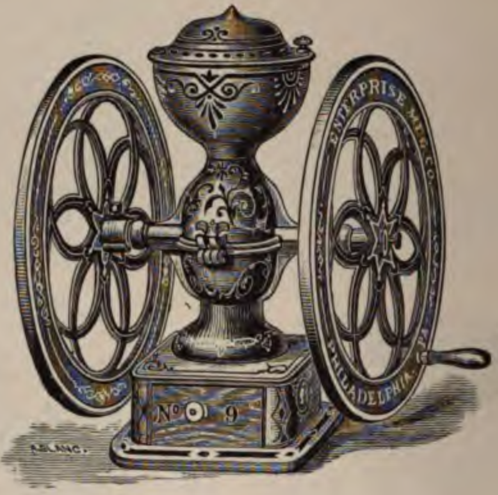


The mill ready for use. The mill open.

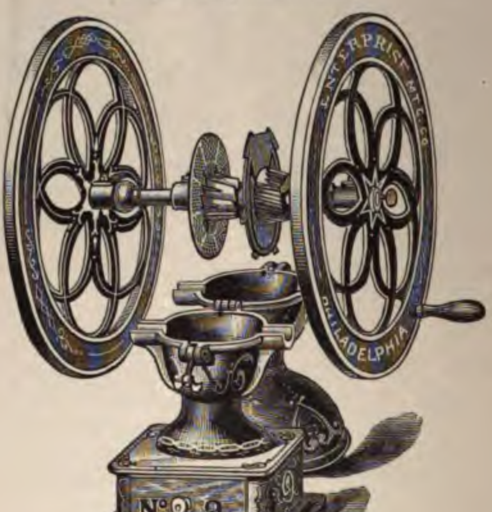
New *B* Swift mill.

Separate sets of plates for coarse and for very fine grinding can be had for the mills. Care should be taken to clean the mill thoroughly after each operation, else the remaining dust will surely contaminate the drug next ground. The simplest method of cleaning is to run sawdust through the mill repeatedly; then loosen the screws and remove the grinding plates, so as to wash these with hot water, if necessary, and dry quickly. A great mistake often made by the inexperienced is the attempt to produce fine powders at once by screwing the plates close together, instead of grinding the drug coarsely at first and gradually tightening the mill; the first plan is apt to cause the material to become heated and cake, while the second plan will achieve the desired end more perfectly, with far less expenditure of manual labor and wear of machinery. Fig. 89 represents the well-known Hance drug mill, having conical grinding

Fig. 88.


ENTERPRISE MFG. CO.
PHILADELPHIA, PA.
No 9

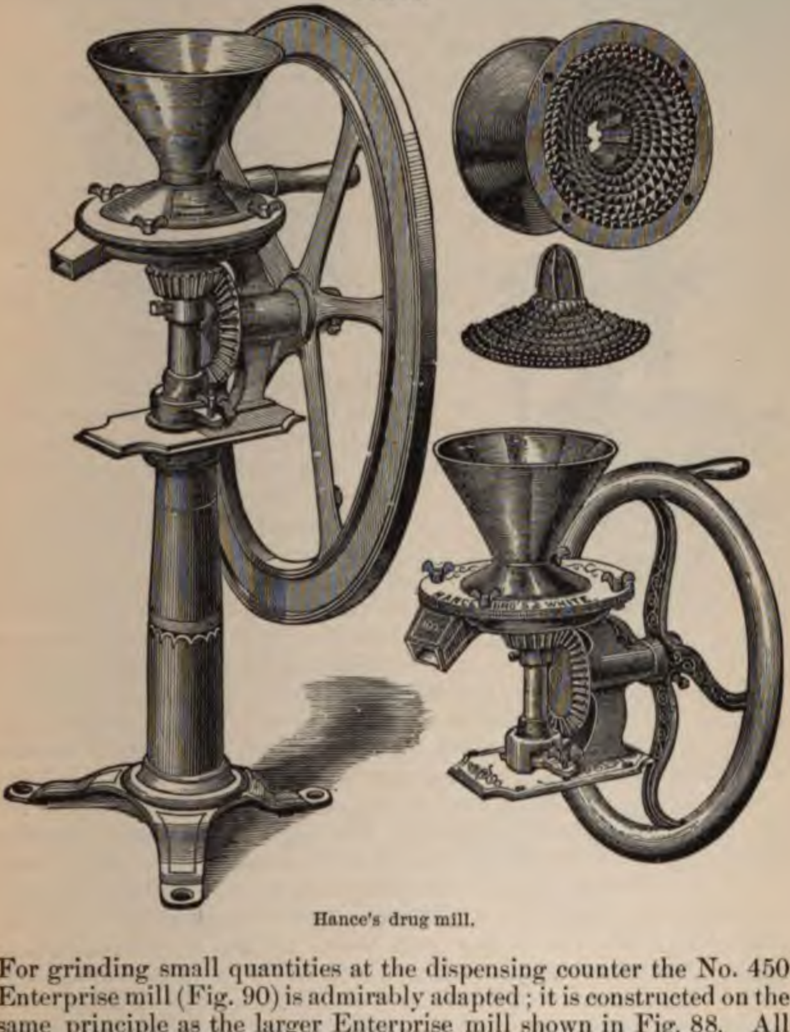
Enterprise drug mill (closed).



Enterprise drug mill (open).

plates, which possess the advantage over the usual styles of not allowing any material to pass through the mill unground (this sometimes happens with vertical plates), and of not holding any of the ground material too long, whereby clogging may sometimes be caused with the horizontal plates. The mill is provided with an iron support, or may be had without it, to be mounted on a heavy block or box.

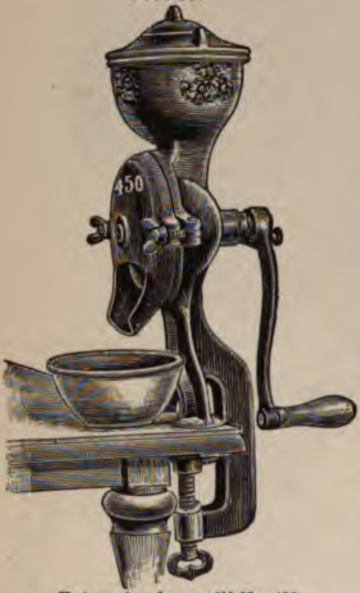
Fig. 89.



Hance's drug mill.

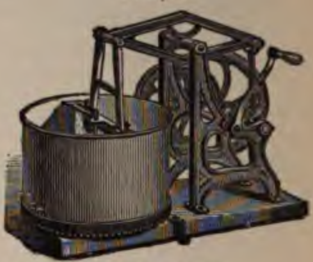
For grinding small quantities at the dispensing counter the No. 450 Enterprise mill (Fig. 90) is admirably adapted; it is constructed on the same principle as the larger Enterprise mill shown in Fig. 88. All the before-mentioned hand-mills can be opened horizontally, as shown in the illustrations, by means of a thumb-screw and hinge; thus the interior may be readily exposed to view for examination or cleaning. The material is supplied through a capacious hopper, with its base specially arranged for crushing the drug into coarse particles. The rapidity with which the material should be fed to the mill depends entirely upon the character of the drug, as some drugs will soften under the influence of heat and pressure, while others are not affected at all. Substances like vanilla, which cannot be heated before powdering, on account of the rapid loss of the aromatic principle, must be reduced in the soft condition; and, although the old method of grinding with sugar or clean sand is still largely in use, it is decidedly inferior to the process of cutting. Grinding or powdering vanilla has a tendency to press out the soft pulp, which soon retards the reduction of the tough fibre and requires the expenditure of much time and labor. If vanilla be reduced to the requisite degree of fineness for percolation by means of a rapid-acting cutter, it retains practically its original condition, no pulp being expressed, and a powder is obtained far superior to that by grinding with sand or sugar. Fig. 91 represents the American mince-meat chopper, an apparatus admirably adapted to the cutting of vanilla, and first suggested for this purpose, many years ago, by the late N. H. Jennings, of Baltimore. The large knife-blade with which the cutting is effected must be kept well sharpened. As the cylinder revolves with each turn of the lever, fresh particles of the material are continually presented to the knife, and disintegration is rapidly achieved, while the aroma and virtue of the vanilla are kept intact.

FIG. 90.



Enterprise drug mill No. 450.

FIG. 91.



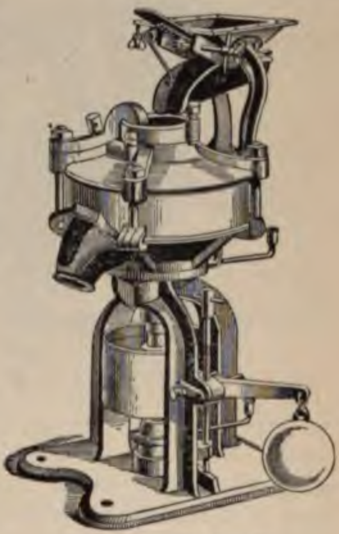
Cutter for vanilla.

The grinding of drugs on a large scale, and particularly into very fine powder, is accomplished either in buhr-stone mills, iron mills, such as the Bogardus eccentric mill, or stone "chaser" mills. In the first-named mill grinding is effected between two large stone disks placed horizontally and provided with numerous furrows to facilitate the passage of the ground drug from the centre to the circumference; one of the disks is stationary—in some mills the upper, and in others the lower—while the other revolves, the material being fed through an opening in the centre of the upper stone. By suitable approximation of the stone disks powders of various degrees of fineness can be produced.

Substances liable to become heated and to cake when ground in ordinary mills, such as vegetable extracts, pepsin, etc., can be reduced to an impalpable powder in the so-called pebble mills now in use by all the leading manufacturers of pharmaceutical preparations. These mills do not crush or cut the material, but grind principally by friction, the effect being produced by the sliding, tumbling, and rolling inside of a stone cylinder, encased in iron, of a large number of flint pebbles, of about the size of duck eggs, mixed with the substance to be ground; the movement is caused by revolving the cylinder at a regulated but slow rate of speed—from 25 to 45 revolutions per minute.

The portable Bogardus eccentric mill (Fig. 92) is a great favorite with drug-millers, as it can be driven at a high rate of speed without becoming heated, and discharges the ground material promptly without danger of choking. Both grinding plates revolve in the same direction, on centres which are about one or two inches apart from each other, hence the name *eccentric;* this arrangement causes the material between the plates to be moved about in every conceivable manner, to be acted upon by the plates at every point, and subjected to a peculiar twisting, cutting, and grinding motion, whereby it is rapidly disintegrated, with large results in quantity ground and the expenditure of but little power. In mills with single revolving plate (the other being stationary), one plate continually describes the same circle on the other, so that material ground in these mills is subject to motion in one direction only, hence greater power and more time are necessary to accomplish the desired result than if the material were acted upon in various directions and by different motions. The rate of feeding the mill is controlled by an adjustable slide attached to the hopper, and the degree of fineness of the powder is regulated by means of a screw and lever controlled by a weight.

FIG. 92.

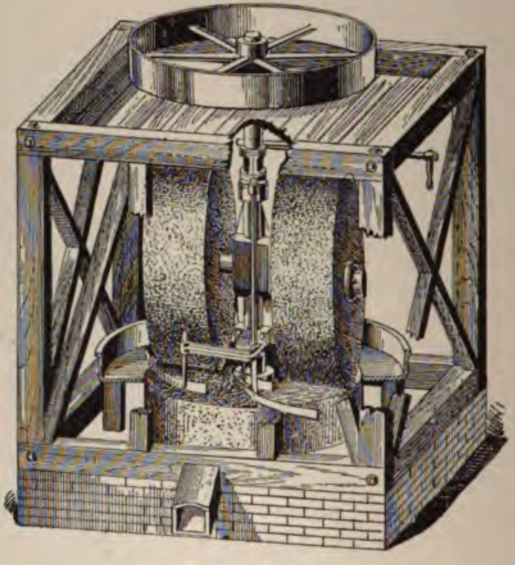


Bogardus eccentric mill.

The so-called chaser mill is preferred when large quantities of material, such as cinnamon, ginger, pepper, mustard-seed, and the like, are to be reduced to impalpable powder. Fig. 93 shows a sec-

tional view of a large chaser mill in use at the drug mills of M
Gilpin, Langdon & Co., of Baltimore. It consists of two large
disks, or granite wheels, connected by a short metallic axle w
revolving shaft, which compels them to travel in fixed lines
base of granite. The name *chaser mill* is derived from the moti
the disks—called *chasers*—which appear to chase each other in
travels over the stone base. The grinding of any material sup
to the mill is effected between the granite base and the outer ed
the chasers; by means of iron scrapers appropriately fastened t
revolving shaft the material is continually brought under the gr
ing edges again. As seen in the illustration, the base is surrou
by a curb, to prevent the coarsely ground particles from mixing

FIG. 93.



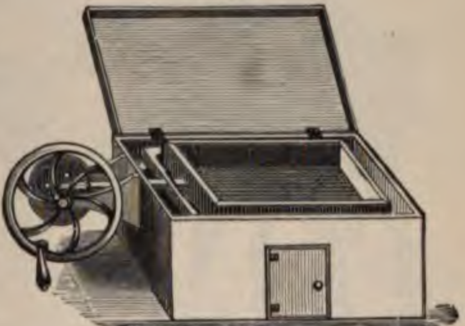
Chaser mill.

the finer powder, which, by means of the draught created by
rapid revolution of the chasers, is carried upward and over the
of the curb. The whole mill is enclosed in a dust-proof com
ment, which is frequently provided with a series of shelves for
purpose of allowing the fine particles of powder to be deposited
subsequent convenient collection. The feeding of the mill is ac
plished through the top of the box, by means of a long funnel d
ering the material directly upon the stone base.

Sifting.—In order to produce powder of uniform fineness
ground substance should be subjected to the separating actio
some perforated medium, whereby division into coarser and
particles is readily effected. The construction of ordinary si

is too well known to require special description. The perforated material or netting used may be made of iron, brass or tinned wire, hair-cloth for substances affected by metal, and silken cloth for very fine or dusted powders. Different degrees of fineness of powder are designated by numbers which indicate the number of meshes to the linear inch in the material of which the sieve is made, and since the diameter or gauge number of the wire used for making the sieve-cloth has an important bearing upon the size of the mesh, it should also be specified. The U. S. Pharmacopœia recognizes *very fine* or No. 80 powder as one passing through a sieve made of No. 38 gauge wire and having 80 meshes to the linear inch; *fine* or No. 60 powder should pass through a sieve made of No. 36 gauge wire and having 60 meshes to the linear inch; *moderately fine* or No. 50 powder should pass through a sieve made of No. 35 gauge wire and having 50 meshes to the linear inch; *moderately coarse* or No. 40 powder should pass through a sieve made of No. 33 gauge wire and having 40 meshes to the linear inch; *coarse* or No. 20 powder should pass through a sieve made of No. 28 gauge wire and having 20 meshes to the linear inch. While it is impossible to grind drugs entirely of the degree of fineness required for many purposes, the aim should be to keep the finer portion down to a low percentage by frequent sifting; not more than $\frac{1}{4}$ of the powder should pass through a sieve having 10 more meshes to the linear inch. It should also be borne in mind that some parts of the drug can be ground more readily than others; it is therefore necessary to mix the powder thoroughly after the grinding and sifting have been completed. The proper handling of a sieve cannot be definitely described, it must be taught practically; this much, however, can be said—that no effort should be made to force the material through the meshes of the sieve by persistent pressure of the hand, which will cause the meshes to open farther and allow coarser particles to pass through. In Fig. 94 is shown the well-known Harris sifting machine, which at one time was extensively used by pharmacists; its construction is very simple and readily understood. Of late years, sifters and mixers combined in one piece of apparatus have been preferred; such a combination, admirably adapted to the wants of the pharmacist who manufactures on a small scale, is shown in Fig. 95. Its capacity is 50 pounds, and the mixer is provided with a galvanized double spiral agitator so arranged that when the sifted powders come in

FIG. 94.



Harris' sifting machine.

contact with it the inside spiral carries the material one way, while the outside spiral carries it the other; thus a most thorough mixture is effected in a short time. After the powders have been mixed, the contents may be withdrawn by means of a slide in the bottom of the circular mixer. Smaller and larger sizes of the "Lightning" sifter and mixer are manufactured, and can be supplied with sieves of different degrees of fineness. Fig. 96 represents Jones' mixer and sifter, in which the mixing is effected on a different principle, by means of paddles and brushes; its capacity is 10 pounds. These combined sifters and mixers are well adapted for the manufacture of Seidlitz mixture, tooth-powder, compound licorice powder, etc., without the annoyance of dirt and dust.

Powdered drugs are frequently offered at prices lower than those asked for a good quality of the crude drug; yet it is well known that the cost is enhanced by loss in drying and powdering, expense of grinding (from 3 to 10 cents per pound), and other incidentals. There can be but one explanation for this anomaly: either an inferior quality of drug has been ground, or admixtures have been made to increase the yield of the powder. According to Squibb, the average loss by powdering (and subsequent drying) of the following drugs has been found to be for

Fig. 95.

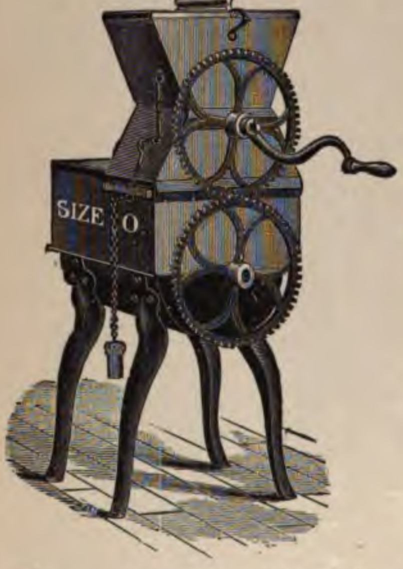
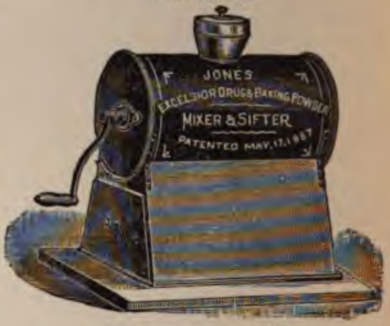


Fig. 96.



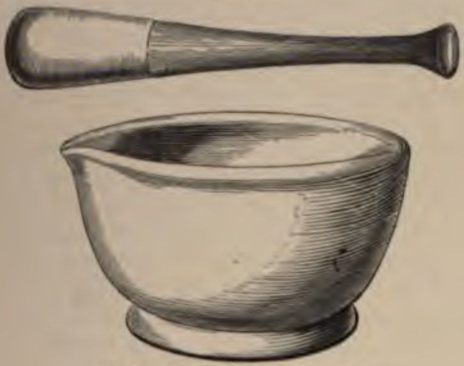
Jones' mixer and sifter.

Acacia,	0.8	per cent.	Ginger (peeled),	9.70	per cent.
Aloes (Socotrine),	17.31	"	Ipecac,	1.91	"
Buchu,	2.00	"	Jalap,	9.58	"
Cantharides,	2.05	"	Myrrh,	5.80	"
Cardamom,	6.02	"	Opium,	19.61	"
Catechu,	1.08	"	Podophyllum,	0.75	"
Cinchona (red),	1.58	"	Rhubarb.	1.74	"
Cinchona (yellow),	2.57	"	Sarsaparilla,	0.70	"
Cinnamon (cassia),	2.61	"	Scammony,	2.70	"
Cubeb,	2.40	"	Squill,	13.60	"
Ergot,	3.62	"	Tragacanth,	6.93	"
Gentian.	10.23	"	Valerian,	1.48	"

Owing to the largely increased surface exposed to light and air in the case of powdered drugs, they are, as a rule, more liable to deterioration than crude drugs, and should therefore be more carefully protected against moisture.

Among other methods for the mechanical subdivision of drugs may be mentioned *trituration*, which consists in reduction of a substance to very fine powder by continued attrition of the particles between the hard surface of a pestle and the sides and bottom of a mortar. Trituration is usually applied to saline and similar chemical substances, and the mortars best adapted to the process are those made of Wedgewood ware, of the shape shown in Fig. 97. A rotary motion of the pestle accompanied by pressure is productive of the best results in trituration, the circles described being gradually enlarged from the centre outward and back again to the centre. A thin layer of the material should be kept between the pestle and the sides of the mortar. When the powder begins to cake and fall toward the centre of the mortar a spatula should be run around the sides so as to loosen up and mix the different portions. The term trituration is also sometimes employed to designate the thorough mixture of vegetable or other powders by rubbing them well together in a mortar; in such cases little if any pressure is employed, and thorough blending of the mixture is facilitated by frequently scraping the powder from both pestle and mortar with a spatula.

FIG. 97.



Wedgewood mortar and pestle.

The reduction of substances to fine powder by triturating them in the presence of a liquid having no solvent effect upon them is termed *levigation*. The process is usually conducted in broad, shallow mortars. Formerly, when a stone slab and muller were employed, this method was also known as porphyrization, from porphyry, a very hard stone, the material of which the slab was made. Water, alcohol, or oil may be used as a suitable medium for levigation, the process consisting of the formation of a paste of the substance to be powdered and the liquid, this paste being then triturated or ground until perfectly smooth. Red mercuric oxide may thus be reduced to an impalpable powder by trituration with alcohol; and white paints, such as zinc oxide and lead carbonate, are ground smooth with oil in special paint mills.

Elutriation is a process intended for obtaining certain inorganic substances in a finely pulverulent condition, by diffusing them in water after they have been ground or crushed; the coarser particles then rapidly subside, owing to their higher specific gravity, while the water holding the fine powder in suspension is decanted and allowed to settle in another vessel, the decantation being repeated a second time if necessary. To facilitate drying of the elutriated powder, the magma or soft mass is drained as completely as possible, and then formed into small conical nodules, which are conveniently dried on warm porous tiles. The well-known soft prepared chalk, French bismuth subnitrate, and numerous lake colors, are obtained as fine powders by elutriation.

Other methods for the mechanical subdivision of drugs are *precipitation*, *reduction*, and *granulation*.

By *precipitation* is understood the sudden destruction of the soluble form of a substance which is held in solution; this may be effected by the addition of another substance to the solution, or by some external agency. The substance thus thrown out of solution is termed the *precipitate*, and the substance or force causing the separation—the *precipitant*. Precipitation is employed in pharmacy as a method of pulverization and purification, and as a convenient means for obtaining many insoluble substances.

The first of these comes under the head of what may be termed simple or physical precipitation, usually brought about by the addition to the solution of some substance in which the dissolved body is insoluble; as in the precipitation of ferrous sulphate or of tartar emetic from aqueous solution by means of alcohol. Other examples of physical precipitation are the separation of iodine or camphor from alcoholic solution by the addition of water, the precipitation of solution of acacia by alcohol, the precipitation of lime-water by boiling, and the preparation of the official resin of jalap.

The process of precipitation when intended as a means of purification or of the preparation of insoluble compounds almost invariably involves chemical action, as in the purification of metals by electrolysis, the manufacture of mercuric iodide, etc.; in the former case simple decomposition of a salt is effected, while in the latter case mutual decomposition between two salts is as a rule necessary.

Some insoluble compounds are precipitated by simple decomposition of a substance by means of water, as bismuth subnitrate, yellow mercuric subsulphate, etc.; in the former case an acid solution is freely diluted with water, in the latter case white mercuric sulphate is thrown into boiling water.

Mercuric oxide can be obtained in a much finer state of division by precipitation than by any other method, but it must be brought about by chemical action. If a solution of mercuric chloride be poured into a solution of sodium or potassium hydroxide two new compounds, yellow mercuric oxide and sodium chloride, are formed, the latter remaining in solution, while the former separates as an impalpable powder, being insoluble in all neutral liquids. Lead iodide, magnesium carbonate, ammoniated mercury, and precipitated chalk are familiar examples of compounds prepared by chemical precipitation.

The character of the precipitate depends largely upon the conditions under which its formation is effected; thus, concentrated solutions are apt to yield dense precipitates, particularly if heat be employed, whereas cold dilute solutions, as a rule, produce light bulky precipitates. In the preparation of new chemical compounds by precipitation it is important that the proportion in which the precipitant is to be employed should be determined by calculation, as a deficiency or an excess may result in loss from imperfect precipitation or re-solution of the precipitate. Mutual decomposition between two salts always takes place in definite molecular proportions, and the necessary quantities may be readily ascertained by writing out an equation showing the decomposition; thus the formation of yellow mercuric oxide is demonstrated by the equation $HgCl_2 + 2NaOH = HgO + 2NaCl + H_2O$, which shows that 1 molecule or 268.86 parts of mercuric chloride requires 2 molecules or 79.52 parts of sodium hydroxide for complete precipitation. In this case an excess of sodium hydroxide is not hurtful, but a deficiency would result in the production of mercuric oxychloride of brownish color instead of a pure yellow oxide. The equation $HgCl_2 + 2KI = HgI_2 + 2KCl$ shows that in the formation of red mercuric iodide 2 molecules or 329.52 parts of potassium iodide are necessary for the complete precipitation of 1 molecule or 268.86 parts of mercuric chloride; these proportions must be strictly observed, otherwise a loss will result, as red mercuric iodide is soluble in both potassium iodide and mercuric chloride solutions. When precipitation by mutual decomposition between two salts is proposed, the salts are mixed in the form of separate solutions, and perfect blending is accomplished by stirring the mixture.

The most convenient style of vessel for precipitation is a glass or stoneware jar considerably broader at the base than at the top, and provided with a lip; this greatly facilitates the subsidence of the precipitate, and the subsequent removal of the clear liquid remaining above the precipitant, known as *supernatant* liquid.

The purification of precipitates is effected by a process of washing, which consists either in mixing them repeatedly with fresh portions of water in a suitable jar, and decanting the supernatant liquid after it has become perfectly clear, or in continued affusions of water on the precipitate contained in a cloth strainer or paper filter; each portion of water should be well mixed with the precipitate and the washing continued until the complete removal of the soluble by-product has been ascertained by appropriate tests. When a precipitate tenaciously retains liquid, forming a thin paste, the mixture is termed a *magma*, and forcible expression must frequently be resorted to in order to remove the liquid, as in the case of washing ferric hydroxide, freshly precipitated calcium phosphate, etc.

The official reduced iron is an instance of a metal obtained in a finely divided state by *reduction ;* ferric oxide being heated to redness in an atmosphere of hydrogen, in suitable tubes, and allowed to cool without contact of air. This method of producing metallic iron in fine powder yields better results than any other known.

Granulation is a process by which certain substances soluble in water are obtained in the form of coarse powder by simple evaporation of their solution, with constant stirring, until all moisture is dissipated. It is employed either for deliquescent and difficultly crystallizable substances, as potassium citrate and carbonate, or in cases where the solution, if allowed to evaporate very slowly, would yield larger crystalline masses, as ammonium chloride, lead acetate, etc. Granulated powders, as the name indicates, never represent a fine state of division, but offer a very convenient form for dispensing and manufacturing purposes. Zinc and tin may be readily granulated in the metallic state by heating them to a temperature a little below their melting-point, when they become very brittle, and can then be rubbed into coarse powder in a mortar.

Some substances obstinately resist pulverization by any of the methods mentioned, and require a different treatment ; for instance, camphor cannot be reduced to a fine powder without being first brought to a state of partial or perfect solution by means of alcohol; a smooth paste being first formed of camphor and alcohol in a mortar; which is then triturated until perfectly dry and in the form of an impalpable powder; excessive pressure should be avoided during the trituration. Powdered camphor thus prepared is prone to return gradually to a crystalline condition no matter how carefully it is preserved, but this can be prevented by precipitating the camphor in the presence of some powder with which it will become intimately mixed. Such a process was first published in Parrish's *Treatise on Pharmacy*, and is as follows: 4 ounces of camphor dissolved in 8 fluidounces of alcohol are poured slowly, with constant stirring, into a smooth mixture of 16 grains of calcined magnesia and 2 pints of water; the precipitated camphor, enveloping the magnesia, soon rises to the surface, and is recovered by pouring the whole mixture on a paper filter, where it is allowed to drain. To facilitate drying of the mass, it is cut with a spatula into small particles, and is finally preserved in bottles. Although retaining a very small amount of moisture, this precipitated camphor keeps excellently, and may be used for all purposes requiring camphor, except cases of solution. Iodoform and boric acid can also be quickly reduced to an impalpable powder by trituration with alcohol, whereby partial solution is effected, and a dry powder is obtained upon evaporation of the alcohol. Friable substances, which are not held together by strong cohesive force, but the particles of which are likely to cake when submitted to pressure, may be powdered by simple friction over a perforated surface; no better method is known for obtaining magnesium carbonate in an impalpable condition than by rubbing the cakes over the surface of an inverted bolting-cloth sieve.

CHAPTER VII.

SOLUTION.

WHEN a solid body is brought into contact with a liquid in such an intimate manner that it loses its original form and assumes that of the liquid, producing a clear and uniform fluid, the process is termed solution, as is also the newly formed homogeneous liquid. The process of solution, however, is by no means restricted to the liquefaction of solids by fluids, as gaseous and liquid substances can also be brought to the condition of perfect molecular blending characteristic of solution; examples: glycerin and water, alcohol and water, castor oil and alcohol, olive oil and chloroform or ether, balsam of Peru and alcohol, chlorine gas and water, ammonia gas and alcohol or water. Some solid substances when brought into intimate contact by trituration with certain other solids also produce clear, uniform liquids, and such interaction is termed solution, as in case of camphor and hydrated chloral, camphor and salol, or camphor and thymol. The fluid used to produce solution is called a solvent or menstruum, the latter name being derived from the Latin *menstruus*, meaning monthly (from *mensis*, a month), and was applied because of some influence which the changes of the moon, and consequently the time of the month, was supposed to exert upon the preparation of solvents. The view at present held by scientists regarding the electro-chemical decomposition of bodies in a state of solution need not be considered here; by some the process of solution is looked upon as one of great force and activity, and this view may in the course of time clear up many hitherto unexplained phenomena.

Two kinds of solution are recognized, namely, *simple* and *complex* solution; in the former the solvent produces no change in the sensible characteristics of the dissolved body, simply altering its physical condition, while in the latter, where solution takes place as the result of chemical action, the properties of both the solvent and the dissolved body become modified by the loss of old or the acquisition of new properties. In the case of a simple solution, the taste, odor, color, and chemical properties of the dissolved body remain intact and are imparted to the solution; as, for instance, solutions of sugar, table-salt, or potassium permanganate in water. In simple solutions the dissolved body can be recovered in its original condition by evaporation of the solvent. Complex solutions should not be confounded with compound solutions; the latter term indicates a mixture of solutions which may all be simple in character, while complex solutions are understood to be the result of chemical action, and are accompanied by one or more of the following phenomena: heat, effervescence, change of color, odor, and taste; as, for example, the solution of a Seidlitz powder or the solution of red mercuric oxide in nitric acid. The products obtained by evaporation of a complex solution will be found to have properties not possessed originally by the solvent or the dissolved body.

The greater the extent of surface exposed by the solid body to the liquefying action of the solvent, the more rapidly will solution be effected; hence mechanical division facilitates solution, because the latter process is in direct opposition to cohesion. A simple solution of solid substances may be considered as a fluid produced by the intimate union of the solvent and the dissolved body in a state of minute division, the union and division being so complete that the forces of cohesion and gravity are suspended, otherwise a mixture only is produced, and the solid substance will again separate. The agitation of a mixture of a solid substance and solvent also causes more rapid solution, by constantly bringing fresh portions of the fluid into contact with the solid; if equal weights of acacia or sugar, in lumps or in fine powder, be placed in separate vessels with a sufficient quantity of water, the one being actively stirred while the other is allowed to remain at rest, solution will be completed in the former vessel long before it occurs in the latter; this is due to the fact that in the second vessel a dense solution will form immediately around the solid particles, and thus prevent the remainder of the fluid from exerting its solvent action.

The simplest way of effecting solution of solids is to bring them in the form of powder into contact with the solvent in such a way that frequent agitation of the mixture is possible; for saline and similar substances a porcelain or Wedgewood mortar, which admits of active trituration, is best adapted. Considerable saving of time may be effected in the solution of larger quantities of solids, if the powdered substance be repeatedly triturated with fresh portions of the solvent, each portion of solution being poured off when saturated. Small quantities of readily soluble substances, such as potassium iodide and bromide, silver nitrate, zinc sulphate, and the like, may be placed directly in a bottle with the solvent, and the mixture agitated until perfect solution results. Some substances, of hygroscopic or deliquescent character, are preferably not reduced to powder before adding the solvent, in order to avoid agglutination; such are the official scale salts of iron, which will dissolve more speedily if shaken with water in scale form than in fine powder. Whenever heat must be employed for small operations of solution, a glass flask will be found more desirable than a dish, as evaporation of the solvent will be retarded, and consequently the heat become concentrated in the vessel. Solutions of solids are known to be denser than the solvents used in preparing them, and advantage is frequently taken of this fact to facilitate the solution of large quantities of solid substances, or of such as are liable to form viscid solutions, or, where stirring or agitation is impracticable, by what is commonly known as *circulatory displacement*, which consists in suspending the soluble matter just below the surface of the solvent, either on a porous diaphragm, in a bag of loosely textured cloth, or in a perforated vessel, which should be moved about from time to time. By this arrangement, that portion of the solvent least charged with soluble matter is always in contact with the solid, and as the solution becomes saturated it sinks to the bottom, displacing the portion less charged with the solid, which rises to the surface, and thus a continual circulation or system of currents, favorable to rapid solution, is kept up in the fluid.

Heat, as a rule, favors the solution of solids and diminishes the solubility of gases, but there are no substances totally insoluble in the cold which become soluble by the aid of increased temperature. The effect of the application of heat is the establishment of currents in the liquid which facilitate solution, just as agitation of the vessel favors the same result; and moreover, since heat intensifies molecular motion in both the menstruum and the solid, not only will an increased quantity of the latter assume the fluid state, but solution will also be effected in less time, on account of the energetic intramolecular activity. There are some exceptions to the general rule that heat increases the solubility of substances; for instance, common salt is about as soluble at ordinary temperatures as at the boiling-point of water; sodium sulphate, or Glauber's salt, increases in solubility rapidly from 15° C. (59° F.) to 34° C. (93.2° F.), at which point water takes up 4 times its weight of the salt, but beyond this temperature its solubility again decreases until 100° C. (212° F.) is reached, when water takes up about 2.13 times its weight of the salt; calcium citrate and sulphate as well as slaked lime are far less soluble in hot water than in cold, and will be readily deposited if their solutions be boiled.

The term "solubility," when no solvent is mentioned, always refers to the behavior of the substance toward water at the ordinary temperature—about 15.6° C. (60° F.); thus the statements that sugar is soluble and bismuth subnitrate is insoluble refer solely to the liquefying effect which water has upon the two substances. Different degrees of solubility are expressed by such terms as *sparingly soluble*, *soluble*, and *very soluble;* these varying degrees of solubility do not determine the rapidity of solution, for some substances are known to dissolve slowly but to a greater extent than others which enter into solution more rapidly but in less proportion. Substances differ greatly in their solubility in water; as extremes may be mentioned zinc chloride, soluble in one-third of its weight of water, and barium sulphate, which requires about 800,000 times its weight of water for solution. Substances but slightly soluble in water may be very soluble in other liquids; as camphor, which requires about 1000 parts of water for solution, but is readily soluble in one-third of its weight of chloroform.

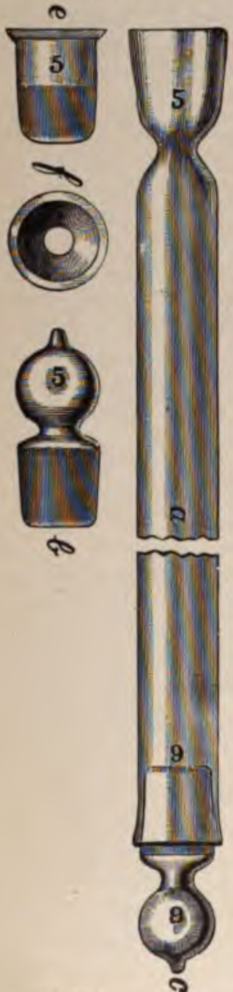
The Pharmacopœia, in the case of nearly every soluble substance, indicates the degree of solubility by stating the number of parts by weight of the solvent necessary to dissolve one part of the substance; this proportion is usually given for both normal and boiling temperatures. The pharmacist must be familiar with the methods for determining the solubility of substances, so as to be able to apply the official tests intelligently. At ordinary temperature, 15° C. (59° F.), a simple but accurate plan is to place some of the substance in fine powder in a wide test-tube, or small flask, provided with a stopper, and add as much of the solvent as may be necessary, leaving, however, a small portion of the substance undissolved; shake the flask freely, or stir the contents of the tube briskly with a glass rod, warm the mixture slightly in a water-bath and allow it to cool down to 15° C. (59° F.), by placing the tube or flask in water having that temperature. In order to avoid a supersaturated solution, the mixture should next be set aside for twenty-four hours at normal temperature, and occasionally stirred with a glass rod, the sides of the tube or flask being also rubbed with the rod. The solution thus obtained is passed through a small dry filter into a tared glass or porcelain dish, and weighed; after evaporation to dryness the residue is carefully weighed, when the difference between the weight of the solution and that of the dry residue represents the weight of solvent, and from this the ratio of solubility is easily calculated. Examples: Suppose the clear filtrate weighs 10.5 Gm. (or 162 grains) and the dry residue therefrom 1.125 Gm. (or 17.36 grains), then the weight of the solvent must be 9.375 Gm. (or 144.64 grains), and the substance under examination is soluble in 8.33 + parts of the liquid used, for $9.375 \div 1.125$ or $144.64 \div 17.36 = 8.33 +$.

It is not necessary that all of the filtrate be evaporated, as a portion of it will yield as accurate results as the whole quantity; but it should be borne in mind that in many cases, especially of solutions of alkaloidal salts, it frequently happens that a paper filter abstracts some of the dissolved substance from the solution, which would, of course, give rise to error; to avoid this, such solutions may be filtered through a pledget of asbestos or glass wool, or if filtered through paper the first third of the filtrate should be rejected and the remainder collected separately.

The determination of the solubility of a substance at temperatures above the normal becomes more difficult on account of the loss incurred during the filtration of hot liquids by ordinary methods. The late Dr. Charles Rice devised a very useful and simple apparatus, called by him a lysimeter (from the Greek *λύσις*, solution), which enables the operator to obtain a clear filtrate without any loss whatever, even at the boiling temperature of liquids. Fig. 98 shows the construction of the lysimeter, which consists of a glass tube, *a*, 15 centimeters (6 inches) in length and 1 centimeter (⅖ inch) in external diameter, provided at one end with a well-ground stopper, *c*, while the other end is cup-shaped, there being a contracted neck between the cup and the main tube. Into this cup is made to fit a carefully ground glass bell, *e*, having a small perforation in its bottom, as shown in *f;* there is also a stopper, *b*, which is carefully ground to fit into the cup, and which is inserted after the glass bell, *e*, has been removed.

When using the apparatus it is necessary to provide sufficient liquid to allow at least one-half of the tube, *a*, to be immersed; beaker glasses, or preferably wide test-tubes, may be used for effecting the solution. Suppose it is desired to ascertain the solubility of a substance in boiling alcohol. The following is the plan of procedure: Insert the stopper *c* into the tube *a*, and into the cup-shaped end insert the glass bell *e*, containing a pledget of purified cotton, and secured in place by a thin platinum wire passing around the contracted neck and over the mouth of the bell. Sufficient alcohol having been put into a wide test-tube or a beaker, the same is heated in a water-bath and the finely powdered substance added until, after boiling has continued for some time, a portion of the substance remains undissolved. The lysimeter, prepared as above directed, is now inserted into the liquid, and when the tube has assumed the temperature of the boiling liquid the stopper *c* is removed, which enables the solution to filter through the pledget of cotton and rise in the tube as far as the quantity of fluid will permit. If the filtered solution be allowed to flow back through the cotton once or twice, greater uniformity of the liquid will be insured. The stopper *c* is now reinserted, the apparatus withdrawn from the liquid and turned upside down to allow the bell *e* to be removed and the stopper *c* to be inserted in its place. The stoppered tube is carefully cleaned externally by washing with alcohol, and laid aside until cold. The tare of the stoppered tube having previously been ascertained, the increase in weight must represent the weight of the solution contained therein. After transferring the solution to a tared capsule or beaker the tube is carefully rinsed with alcohol, and the washings added to the contents of the capsule or beaker; the solution is slowly evaporated on a water-bath, and afterward heated to

FIG. 98.



Rice's lysimeter.

dryness in a drying oven, when the weight of the residue will indicate the weight of the dissolved substance, and subtracting this from the weight of the solution gives the weight of alcohol. From these data the ratio of solubility is calculated in the manner already explained in the example given for determining the solubility at normal temperature.

Rapid simple solution of solid bodies is always accompanied by a fall in temperature, while a solution of gases causes a rise in temperature; these phenomena are in accordance with the laws governing the state of aggregation of bodies. Solids, for the assumption of the fluid state, require a certain amount of energy or heat, which is withdrawn from the surrounding liquid and becomes latent, while gases when condensing to liquids give out an amount of heat corresponding to that required for maintenance of the gaseous state. Four ounces of ammonium nitrate or potassium iodide rapidly shaken in a bottle with two ounces of pure water will produce sufficient cold to condense the moisture of the air on the outside of the bottle and freeze it into thin sheets of ice.

Since rapid simple solution causes a decided fall in temperature, advantage is taken of the fact that some substances hasten the liquefaction of others in the production of so-called freezing mixtures; thus, 5 parts each of ammonium chloride and potassium nitrate dissolved in 19 parts of water will cause a drop of temperature of 20° C. (36° F.); a mixture of 2 parts of snow and 3 parts of crystallized calcium chloride will cause the temperature to fall from 0° C. (32° F.) to —45.5° C. (—50° F.) and freeze mercury; the usual mixture for ice-cream freezers consists of salt with twice its weight of snow or crushed ice, which produces a temperature equal to about —20° C. (—4° F.), the cream in the cylinder freezing by reason of the great abstraction of heat necessary for the rapid liquefaction of the ice and snow surrounding it—not, as some persons believe, because intense cold is imparted to it from the outside.

Salts which have been deprived of their water of crystallization, and thus been converted into anhydrous amorphous powders, will cause a more or less marked rise in temperature when brought into solution; the heat thus generated must be looked upon as due to chemical action involving the restoration of water necessary for the assumption of the crystallized state by the anhydrous salt. If crystallized sodium carbonate be shaken with twice its weight of water, a marked fall in temperature will be noticed, whereas anhydrous sodium carbonate shaken with twice its weight of water causes a rise in temperature, thus proving the correctness of the preceding supposition. When liquids are dissolved in other liquids no change of temperature will occur in the mixture unless contraction of volume takes place, as in the case of alcohol and water or sulphuric acid and water.

Saturated solutions, in a pharmaceutical sense, are such as cannot take up any more of the dissolved body at ordinary tem-

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perature; in other words, the solvent has become charged with as much soluble matter as it is capable of retaining in intimate union at the ordinary temperature. The statements of ratio of solubility in the Pharmacopœia and elsewhere always refer to the formation of saturated solutions at the temperature named; thus the official statement that cane-sugar is soluble at 25° C. (77° F.) in 0.46 part of water and 137.2 parts of alcohol, in $\frac{1}{5}$ part of boiling water and 28 parts of boiling alcohol, means that with the proportions of water and alcohol named sugar forms saturated solutions at the temperatures indicated. Supersaturated solutions are those in which the solvent, by artificial means, has been made to take up more of the soluble matter than it is capable of retaining under ordinary circumstances; they are very unstable and present a peculiar condition of solubility. If 3 parts of sodium sulphate be dissolved in 1 part of water at 30° C. (86° F.), the solution carefully filtered into a perfectly clean dry bottle free from dust, and allowed to cool gradually, it will remain clear as long as it is not disturbed, although supersaturated, since water at 15° C. (59° F.) can dissolve only about one-third of its weight of the salt; but if the bottle containing the supersaturated solution be shaken, or a little broken glass be introduced, the whole contents will suddenly congeal to a crystalline mass. Saturated solutions of salts are frequently capable of dissolving other salts, and thus may be used for purposes of purification; if potassium nitrate be treated with a saturated aqueous solution of the same salt, no more potassium nitrate can be taken up, but impurities present will enter into solution and are thus removed.

The effect which the presence of one substance may have upon the solubility of another is interesting as well as of practical value in pharmacy. Corrosive sublimate is far more soluble in water in the presence of alkali chlorides, and red mercuric iodide is readily dissolved in a solution of potassium iodide; in both cases union takes place between the mercuric and alkali salts. The increased solubility of potassium chlorate in the presence of sodium bicarbonate is well known; mutual decomposition, no doubt, results, the newly formed salts, sodium chlorate and potassium bicarbonate, requiring only 1.1 part and 3.2 parts of water at 15° C. (59° F.) respectively for solution, as against 16.7 and 12 parts for the original salts. Ordinarily iodine requires about 5000 parts of water for solution, but if mixed with twice its weight of potassium iodide it will readily dissolve in 20 times its weight of water. In this case no chemical union takes place, as the iodine has every appearance of being dissolved but not combined; it retains its characteristic color and odor, and if the solution be heated in a test-tube the iodine can be completely volatilized, a portion subliming in the cooler part of the tube in its original condition.

A marked example of the effect of the presence of one substance on the solubility of another is found in the well-known concentrated solution of sodium phosphate, largely used by physicians.

Sodium phosphate contains ordinarily about 60 per cent. of water of crystallization, and is soluble at 15° C. (59° F.) in 6 parts of water; if 100 Gm. of the salt be triturated with 13 Gm. of citric acid and 2 Gm. of sodium nitrate until liquefied, and enough water then added to bring the volume up to 100 Cc., the solution will keep. This solution, which represents about 60 grains of sodium phosphate in each fluidrachm, is the result of chemical action, and is called by some solution of sodium citrophosphate and by others compound solution of sodium phosphate.

In striking contrast to the above examples may be mentioned the insolubility of potassium sulphate in a solution of ammonium sulphate and of potassium nitrate in a solution of ammonium nitrate.

Solutions of solids always measure more than the liquid used to prepare them, but never as much as the combined volumes of the solvent and dissolved body. The increase in volume will naturally vary considerably, and be greatest when the substance to be dissolved is very soluble, as sugar, sodium salicylate, or potassium iodide in water. Another factor determining the volume of the solution is the presence of large proportions of water of crystallization. The following table of saturated solutions, prepared at the temperature of 15° C. (59° F.), is of interest:

Name of Substance.	Quantity of Substance Used.	Quantity of Water Used.	Volume of Finished Solution.
Borax,	6 Gm.	96 Cc.	99 Cc.
Ferrous Sulphate,	40 "	72 "	93 "
Magnesium Sulphate,	40 "	60 "	82 "
Potassium Bromide,	40 "	64 "	77 "
Potassium Chlorate,	5 "	85 "	87 "
Potassium Iodide,	40 "	30 "	42 "
Sodium Bicarbonate,	6 "	68 "	71 "
Sodium Chloride,	20 "	56 "	63 "
Sodium Phosphate,	12 "	72 "	79 "
Sodium Salicylate,	40 "	36 "	61 "
Sodium Sulphate,	20 "	56 "	69 "
Sugar,	60 "	30 "	68 "

(Borax, ferrous sulphate, magnesium sulphate, sodium phosphate, and sodium sulphate contain water of crystallization varying from 45.31 per cent. to 60.3 per cent. of the weight of the substance.)

Percentage Solutions.—This term is applied to solutions of definite strength, containing a specified amount of soluble matter in 100 parts of the solution; thus a 1 per cent. solution is composed of 1 part of the soluble substance and 99 parts of the solvent; or a 5 per cent. solution is composed of 5 parts of the soluble substance and 95 parts of the solvent, etc. For solids and gases percentage solutions should always be prepared by weight, while for liquid substances either weight or volume may be employed. The quantity of soluble substance and solvent necessary to make a specified quantity of any particular percentage solution may be readily ascertained by the following rule: *Multiply the quantity of solution desired, in* *grammes or grains, by the number expressing the percentage, divide the product by* 100, *and the quotient will indicate the quantity of soluble substance necessary; subtract this from the total quantity of solution desired, and the remainder will indicate the necessary quantity of solvent.*

Examples: Wanted 500 Gm. of 10 per cent. carbolized oil: 500 × 10 = 5000, and 5000 ÷ 100 = 50; 500 — 50 = 450. Answer: Dissolve 50 Gm. of crystallized carbolic acid in 450 Gm. of olive oil.

Wanted 750 grains of 4 per cent. cocaine hydrochloride solution: 750 × 4 = 3000, and 3000 ÷ 100 = 30; 750 — 30 = 720. Answer: Dissolve 30 grains of cocaine hydrochloride in 720 grains of distilled water.

Wanted 640 Gm. of 2 per cent. mercuric chloride solution: 640 × 2 = 1280, and 1280 ÷ 100 = 12.8; 640 — 12.8 = 627.2. Answer: 12.8 Gm. of mercuric chloride must be dissolved in 627.2 Gm. of distilled water.

Wanted 480 grains of 20 per cent. quinine oleate: 480 × 20 = 9600, and 9600 ÷ 100 = 96; 480 — 96 = 384. Answer: Dissolve 96 grains of quinine alkaloid in 384 grains of oleic acid.

Sometimes a percentage solution of two or three substances is wanted; in such a case the absolute quantity of each active ingredient is first ascertained by the rule given above; the sum of their weights is then subtracted from the total quantity of solution desired to find the necessary weight of the solvent; for instance: Wanted 250 grains of 8 per cent. cocaine hydrochloride solution, containing also 2 per cent. of boric acid: 250 × 8 = 2000, and 2000 ÷ 100 = 20; 250 × 2 = 500, and 500 ÷ 100 = 5; 20 + 5 = 25; 250 — 25 = 225. Answer: Dissolve 20 grains of cocaine hydrochloride and 5 grains of boric acid in 225 grains of distilled water.

When a definite volume of a weight percentage solution is wanted, the quantity nearest in volume to that required must be made; although this sometimes involves a slight loss, there is no other method known if accuracy is to be preserved. Thus, if 2 fluidrachms of a 4 per cent. solution of any soluble chemical are wanted, 5 grains of the substance must be dissolved in 120 grains of water; the 125 grains of solution will measure a trifle more than 2 fluidrachms. If 8 fluidounces of a 10 per cent. solution are wanted, 4100 grains of solution must be made by using 410 grains of the medicinal agent and 3690 grains of water; 8 fluidounces of water weigh 3646 grains, hence the excess of solution will not be large. If a quart of 1 per cent. mercuric chloride solution is desired, 15,000 grains of solution must be made, as the weight of a quart of water is 14,583 grains, which is only 267 grains less than the quantity of water necessary; 150 grains of mercuric chloride dissolved in 14,850 grains of water yield only a little over ½ fluidounce more of the solution than is wanted. If 500 Cc. of a 5 per cent. solution are desired, 530 Gm. of the solution must be made, the excess of solution being 3.5 Cc., for 5 per cent. of 530 is 26.5, and as each Cc. of water equals 1 Gm., 530 — 26.5 = 503.5. When solvents other than water are used, having a higher or lower specific gravity, due allowance must be made for this fact, as the volume of a liquid compared with that of an equal weight of water varies with the specific gravity of the liquid; thus, if 4 fluidounces of a 5 per cent. solution of iodoform in alcohol are desired, it will suffice to make 1600 grains, of which 80 grains must be iodoform and 1520 grains alcohol; this will insure the full volume desired, as the specific gravity of official alcohol is 0.820, and 4 fluidounces will therefore weigh only 1494.7 grains (for $455.7 \times 4 \times 0.820 = 1494.69$), whereas 4 fluidounces of water weigh 1822.8 grains. If a definite volume of a percentage solution in glycerin is required, it becomes necessary to make a larger quantity by weight than for the same volume of an aqueous solution, because the specific gravity of glycerin is 1.25, or one-fourth higher than that of water, while its specific volume is only 0.8, or one-fifth lower than that of water. To make 250 Cc. of a 10 per cent. solution of borax in glycerin would require 35 Gm. of borax and 315 Gm. of glycerin, yielding 350 Gm. of solution; this quantity will not be much in excess of 250 Cc., since the volume of 315 Gm. of glycerin is 252 Cc. ($315 \div 1.25$), and the presence of the borax will not materially influence the volume. When strong percentage solutions of saline substances are made the latter often increase the volume of fluid markedly, and particularly so if they contain much water of crystallization, as shown in the table on page 125.

Solutions of arbitrary strengths are frequently employed, and although not as accurately made as percentage solutions, nevertheless seem to answer the purposes well for which they are intended. They are usually prepared as follows:

Strength of Solution.	Quantity of Soluble Substance Used.	Quantity of Water Used.
1 in 250	1 grain	4½ fluidrachms.
	1 gramme	250 cubic centimeters.
1 in 500	1 grain	9 fluidrachms.
	1 gramme	500 cubic centimeters.
1 in 1000	1 grain	18 fluidrachms.
	1 gramme	1000 cubic centimeters.
1 in 5000	1 grain	11 fluidounces.
	1 gramme	5 liters.
1 in 10,000	1 grain	22 fluidounces.
	1 gramme	10 liters.
1 in 50,000	1 grain	110 fluidounces.
	1 gramme	50 liters.

(It is evident that if metric weights and measures are used, much greater accuracy will be insured.)

The so-called *normal salt solution* used by physicians for transfusion and other purposes must not be confounded with the normal sodium chloride solution used by chemists in volumetric analysis. The former, preferably called *physiological salt solution*, contains but 6 grammes of sodium chloride in a liter, and is practically a 0.6 per cent. solution.

The liquids used as solvents or menstrua in pharmacy are water, alcohol, glycerin, ether, chloroform, and occasionally diluted acids and alkaline solutions, as well as fixed and volatile oils; each of these fluids has a specific action, and their use gives rise to different classes of solution designated as infusions, tinctures, wines, etc. *Water* is more extensively employed than any other solvent; nearly all the salts of the alkalies, earths, and metals are dissolved by it, together with a large number of vegetable acids and the salts of the alkaloids. *Alcohol* is an excellent solvent for vegetable substances, such as resins, volatile oils, glucosides, and alkaloids; it also possesses valuable negative properties, since it does not dissolve gum, starch, and albumen, which impair the stability of aqueous solutions. The combined solvent powers of alcohol and water are utilized in the form of diluted alcohol or wine as a menstruum for numerous liquid vegetable preparations. *Glycerin* is chiefly employed to insure the permanency of vegetable solutions when the use of alcohol is contra-indicated; it is also an excellent solvent for the tannins, pepsin, and some mineral salts and vegetable acids, and forms the basis of a valuable class of solutions known as *glycerites*. The use of *ether* is confined to solutions of fixed oils and fats, volatile oils, and resins, and some alkaloids and neutral principles. *Chloroform* is employed as a solvent for phosphorus, the active constituents of some drugs, as cantharides, as well as the substances mentioned above under ether, possessing the advantage over the latter of non-inflammability and a higher boiling-point. *Acids*, such as acetic, hydrochloric, and sulphuric, are used in connection with water or water and alcohol to facilitate the solution of active principles in drugs like cinchona, nux vomica, ergot, sanguinaria, squill, etc., and also to preserve better the resulting solutions. *Alkalies* are employed as solvents for resinous bodies, but to a limited extent only, and the use of *fixed* and *volatile oils* is restricted to very few substances, chiefly in connection with liniments and ointments.

The process of treating a mixture of soluble and insoluble mineral substances with solvents which only partially dissolve them is termed *lixiviation* or *leeching*, and is extensively practised in the arts; as an example may be cited the leeching of ashes of wood and marine plants for the purpose of dissolving out the alkali carbonates, iodides, etc. The various methods of partial solution applied to mixtures of soluble and insoluble vegetable matter are usually comprised under the general term "extraction," but have received specific names, such as infusion, decoction, maceration, digestion, and percolation.

The process of *Infusion* is understood to represent the solvent action of boiling water on vegetable drugs during the time occupied in cooling; it may be varied, as to a longer or shorter period of time, according to the degree of extractibility of the principles to be dissolved, and should always be conducted in closed vessels. The substance to be infused should be in a coarse state of division and preferably suspended in the liquid. *Decoction* represents the solvent action of fluids at their boiling temperature, and is confined to drugs not yielding their active virtues at a lower temperature and where no loss of volatile principles need be feared. *Maceration* consists in subjecting a mixture of soluble and insoluble matter in a divided state to the solvent action of fluids at ordinary temperature for such length of time as may be necessary to insure complete solution of the principles sought; the process must be conducted in well-closed vessels, and the contents must be well shaken at least once in twenty-four hours. Frequent agitation is essential if complete extraction of soluble matter is to be insured by maceration, as otherwise a dense layer of a concentrated solution will soon envelop the material and prevent the solvent action of the menstruum from being effective; hence only a small proportion of the soluble constituents will be taken up, as may be readily observed in the slight color and odor of the supernatant liquid if a mixture of asafetida and alcohol, or of opium and water, be set aside for a week *without agitation*. *Digestion* differs from maceration only in the higher degree of temperature employed, it being constant during the process, the use of which is confined to substances of very close texture.

CHAPTER VIII.

PERCOLATION.

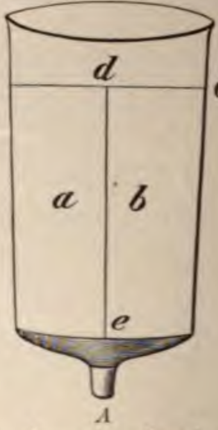
PERCOLATION, or, as it is sometimes called, displacement, is beyond doubt the most important method of solution or extraction in the hands of the pharmacist. The term percolation (from the Latin *per* and *colo*, meaning to strain or trickle through) may be defined as a process whereby the soluble constituents of vegetable drugs are extracted by allowing the menstruum to permeate a column of the more or less finely powdered material, the saturated solution being removed as fast as formed, thus continually presenting fresh solvent to the drug. The apparatus in which the process is carried on is known as the *percolator*, the solution obtained as the *percolate*, and the residue of insoluble matter as the *marc*.

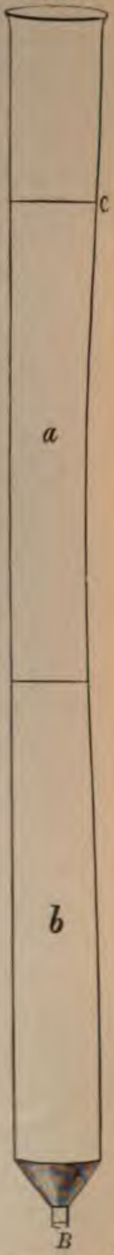
Although the idea of solution by percolation did not originate in this country, its present improved and general application is due entirely to American enterprise and ingenuity. The first attempt to extract soluble matter from powdered drugs by allowing a menstruum to exert its solvent action during its passage through a column of the material was made by Count Real in the early part of the nineteenth century, the principle involved being about the same as that utilized by the French in the preparation of their world-renowned coffee. In 1833 M. Boullay, an enterprising French pharmacist, considerably modified the plan of Count Real, and in a series of carefully conducted experiments demonstrated the adaptability of the process of percolation to the extraction of vegetable drugs. So convincing were the results of his investigations that Prof. William Procter and A. Duhamel, prominent American pharmacists, became deeply interested in the work, and in 1839 strongly advocated its adoption as a method of extraction superior to others known at that time. Although the process of percolation was recognized in the United States Pharmacopœias of 1840 and 1850, it did not meet with the general favor since accorded it until Prof. Israel Grahame, of the Maryland College of Pharmacy, in 1858, suggested some valuable improvements, which led to better results than had yet been obtained. To Prof. Grahame belongs the credit of first advocating the use of powders of uniform degree of fineness as well as the proper moistening of the powdered drug with a sufficient quantity of the menstruum before packing it in the percolator, both of which suggestions are now considered indispensable to successful percolation; at the same time, the use and advantage of a common funnel for the percolation of many drugs was pointed out. The advantage of properly moistening the powdered drug before packing will be readily understood when it is considered that the material to be operated upon is not a mere mechanical mixture of soluble and insoluble matter, but that the soluble principles to be extracted are intimately held or enclosed by the insoluble cellular tissue, and that penetration of the tissue by the menstruum is necessary to effect solution; the saturation of the powder with the liquid prepares the constituents for ready solution and establishes an affinity between the cellular contents and the fresh menstruum, enabling the latter to permeate the cells by osmotic action. If the menstruum is brought in contact with dry powder, absorption of the former either takes place very slowly or is entirely interfered with, just as dry, hard sponge resists the entrance of water for a long time; the original moist condition of the drug before it was powdered must therefore be re-established before the menstruum can exercise its power of extraction.

The principle underlying the process of percolation may be stated as follows: A solvent or menstruum, poured on the top of a mass of powder consisting in part of soluble matter, supported on a porous diaphragm in a cylindrical or conical vessel, descends from layer to layer by reason of its own gravity and the pressure of the superincumbent liquid, penetrating the particles of powder by reason of surface action, and exercising its solvent power on each successive layer until its power of solution is exhausted, after which it continues its downward flow, as a saturated solution, into the receiving vessel below. This process continues until all soluble constituents have been removed from the powder, the descending menstruum becoming less and less charged with extractive matter. To insure such complete extraction it is absolutely necessary that the material operated upon shall be in a uniform powder and that the capillarity or porosity of the mass be not interfered with in any way, so that the descent of the menstruum may be slow, even, and regular from one horizontal layer to the next.

Different styles of percolators have been proposed at various times, and as drugs vary in their nature and require different treatment to yield different preparations, the pharmacist must be supplied with a variety of percolators, from the conical shape of the ordinary funnel to the nearly cylindrical. The choice of percolator depends largely upon the character of the percolate to be obtained, and also upon the nature of the drug; for instance, if a very strong solution is to be prepared with a minimum quantity of menstruum, a narrow cylindrical percolator is preferable, so that the solvent is made to pass through a long column of the drug and thus become thoroughly saturated; a cylindrical, or only slightly tapering, percolator is also indicated when the menstruum is strongly alcoholic, or when ether or some other volatile liquid is used for extraction. The advantage of using a long, narrow percolator with the view of economizing menstruum when concentrated vegetable solutions are to be made, may be easily demonstrated by means of two percolators having the same cubical capacity, but of such difference in shape that the diameter of the one shall be exactly one-half the diameter of the other, and that the narrower percolator shall be four times as long as the other, as shown in Fig. 99, *A* and *B*. Suppose a given quantity of drug is packed into *A* and fills the same up to the line *c*, and then a like quantity of drug be packed into *B*; if we assume the mass in *A* to be divided into two equal sections, *a* and *b*, by means of the plane *de*, it is fair to assume that the same quantity of material in the respective sections *a* and *b* when packed in *B*, instead of occupying adjoining spaces as in *A*, would lie one above the other. If it requires 10 liters of menstruum to exhaust completely the drug in *A*, it may be assumed that the sections *a* and *b* required equal amounts, or 5 liters each. If 5 liters of menstruum be now poured upon the column of drug in *B*, this quantity of menstruum will prove sufficient to exhaust completely the upper section *a*, as the same quantity of solvent proved adequate for the complete exhaustion of an identical quantity of drug in *A*; but the solvent powers of the menstruum will not have been entirely spent, and hence as it passes downward through the lower section *b* it will continue to extract soluble matter until fully saturated, and then flow off into the receiving vessel. All the soluble matter in *a* and a portion of that in *b* having been taken up by the 5 liters of menstruum used, another portion of menstruum is poured on the top of the column, and as there is no soluble matter left in *a*, it will be necessary only to extract the soluble matter still remaining in *b*, for which purpose 2 or 3 liters of menstruum will suffice. Thus in connection with percolator *B*, 7 or 8 liters of menstruum are found sufficient to exhaust completely a quantity of drug which in percolator *A* was found to require 10 liters of menstruum, showing a saving of about 20 or 30 per cent. If, on the other hand, the quantity of

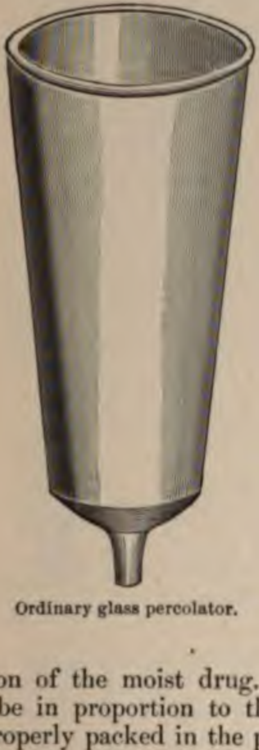
Fig. 99.





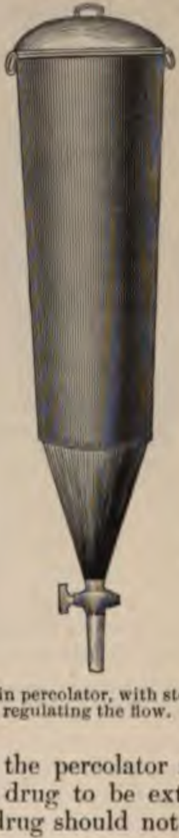
drug to be extracted is small in proportion to the menstruum, as in the majority of official tinctures, a wider percolator, of the shape and style shown in Fig. 100, may be used, in which the liquid will traverse the column of drug more rapidly and yet be able to exhaust it thoroughly, owing to the larger amount of menstruum at the disposal of the operator. When drugs such as gentian, senega, rhubarb, orange-peel, and others, which have a tendency to swell considerably, particularly with aqueous or feebly alcoholic menstrua, are to be percolated, a common funnel will often be found advantageous on account of the ample allowance for lateral expansion of the moist drug. The size of the percolator selected should be in proportion to the quantity of drug to be extracted; when properly packed in the percolator the drug should not occupy more than about three-fourths of its height.

FIG. 100.



Ordinary glass percolator.

FIG. 101.

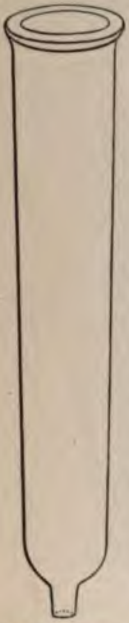


Covered tin percolator, with stopcock for regulating the flow.

The covered tin percolator (Fig. 101) consists of a cylinder varying in size and tapering somewhat toward the funnel-shaped end, provided with two perforated diaphragms fitting loosely into the cylinder, the lower of which should be more finely perforated than the upper. The stopcock in the neck of the funnel serves the double purpose of allowing maceration for any desired period and of enabling the operator to regulate the rate of flow of the percolate. Tin percolators cannot be used, however, for any drugs containing principles liable to be affected by metal, or to be exhausted with acid menstrua.

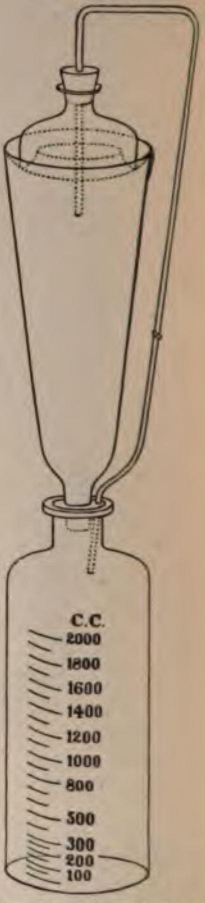
Fig. 102 represents the Oldberg percolator, introduced in 1884, and especially designed for use in the preparation of fluid extracts. These percolators are now made of heavy glass in nine sizes, varying from 240 to 7000 cubic centimeters (about 8 fluidounces to 2 gallons) capacity. They are used extensively, and are admirably adapted for the exhaustion of drugs with a minimum quantity of menstruum.

FIG. 102.



Oldberg percolator.

FIG. 103.

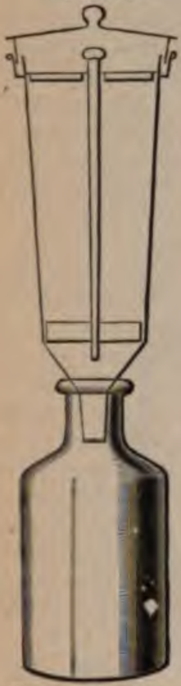


Glass percolator for use with volatile menstruum.

For percolation with very volatile liquids—ether, chloroform, and the like—a specially constructed percolator must be used (see Fig. 103), in which proper provision is made to prevent loss of menstruum and to establish communication between the vessel intended to receive the percolate and the space above the drug in the percolator, so that the air may pass upward when displaced by the percolate in the receiving jar; this latter provision is essential to successful percolation. As may be seen from the illustration, the percolator is fitted air-tight to the receiving vessel by being passed through a cork, and loss of menstruum at the top is prevented by a water-joint with which the cover of the percolator forms an air-tight connection. The air is carried up outside of the percolator, and made to enter at the top, to take the place of menstruum passing downward through the drug. Fresh menstruum may be supplied through the opening in the cover without disturbing the water-joint. Another plan to provide for the upward displacement of the air from the receiving jar is to pass a tube through the centre of the percolator and extending below the lower diaphragm, the drug being packed around the tube; such an arrangement is shown in the tin percolator, Fig. 104, which is likewise provided with a water-joint, and the exit tube of which should also pass air-tight through a cork in the neck of the receiving vessel. An arrangement of tubing on the outside, as seen in Fig. 103, may be attached to any percolator capable of being closed air-tight at the top with a cork.

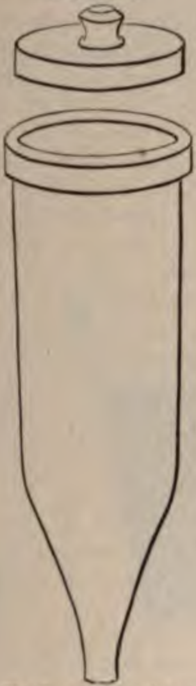
In 1874 the Dursse percolator was introduced (see Fig. 105). It combines the advantages of a broad cylindrical and a conical vessel, and is admirably adapted for quantities of drug ranging from 400 to 600 Gm. Unfortunately but one size is made of this pattern, which is 15 inches in length, 5 inches in diameter at the top, and 1 inch at the beginning of the outlet tube. One of these percolators was in use almost weekly, during eighteen years, in the author's hands, and many pounds of nux vomica, cinchona, ergot, ginger, vanilla, gentian, rhubarb, valerian, etc., were successfully extracted therein during that time. Its chief merits lie in the perfect uniformity of its sides and its accurately fitting cover, by which the flow of the liquid can be regulated and all volatilization of menstruum be prevented. Being made of heavy glass, it bears usage very well and is not easily broken.

Fig. 104.



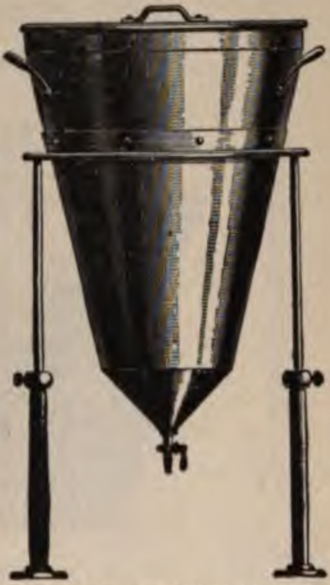
Tin percolator for volatile liquids.

Fig. 105.



The Dursse percolator.

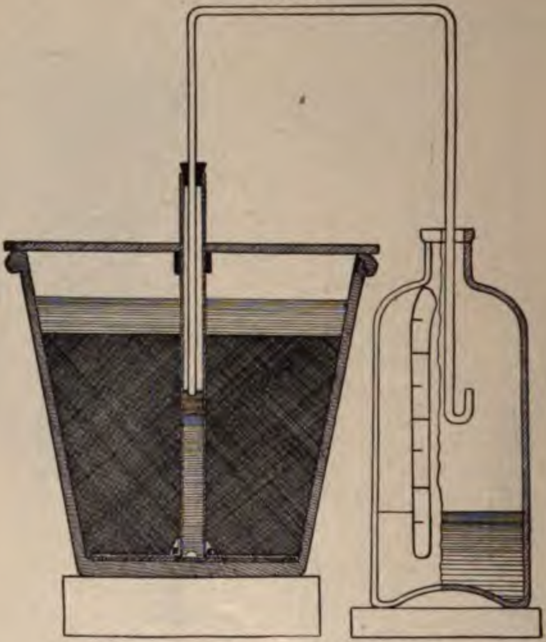
Fig. 106.



Copper percolator, tinned inside. (Capacity, 20 to 100 gallons.)

Manufacturers who operate upon large quantities of drugs, varying from 25 to 500 pounds or more, employ percolators made of heavy tin or tinned copper. Such percolators are usually of the shape shown in Fig. 106, and supported in an adjustable frame; or are cut off flat at the point where the funnel-shaped end begins, and supported on a heavy wooden stand. In the latter shape, the drip-cock is situated on the side of the percolator, near the bottom. These large percolators are provided with two diaphragms or perforated disks, likewise made of heavy tin; the one is placed about 8 or 10 inches from the bottom, and is usually covered with a piece of muslin before the moistened drug is introduced, while the other diaphragm is inserted over the mass of drug, which has been previously covered with a piece of felt or flannel to insure uniform distribution of the menstruum. In order that the descent of the menstruum may be regular and uninterrupted during maceration of the drug, a tube attached to the inner side of the percolator connects the space below the lower diaphragm with the space above the upper disk, and thus allows the air from below to displace the menstruum above. A well-fitting cover, as shown in the illustration, prevents evaporation of alcohol and admits fresh menstruum when desired.

FIG. 107.

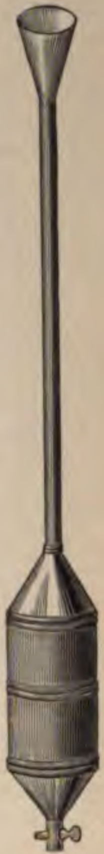


Squibb's well-tube percolator, made of stoneware.

The well-known siphon or well-tube percolator, suggested in 1872 by the late Dr. E. R. Squibb, is extensively used in the laboratories of some manufacturers; the principle involved, with slight modifications, has been adopted in the official direction for percolation in the United States Pharmacopœia since 1880. The Squibb well-tube percolator, as shown in Fig. 107, is constructed upon the principle of an artesian well, the moistened drug representing the soil, through which the menstruum passes very slowly, the solution or percolate, rising in the well-tube which passes through the centre of the mass, being finally drawn off by means of the glass siphon. The process is completely under the control of the operator as regards the rate of flow of the percolate and maceration of the mass to any desired extent. To prevent particles of drug from entering the well-tube, this is made to rest on several disks of flannel, through which the percolate must pass before it can enter the tube. The siphon acts automatically after it has once been started, and cannot exhaust itself, because when the liquid in the percolator falls to the level of the turned-up end of the outer limb of the siphon the flow ceases, leaving the siphon-tube full of liquid, the difference in the length of the two limbs of the siphon being only such that the inner limb reaches the bottom of the well-tube, and when measured on the outer limb, reaches to one-half of its turned-up end. The pressure on the surface of the moistened drug being duly counterbalanced by the atmospheric pressure on the column of percolate in the well-tube and siphon, all particles of the mass in the percolator will be subject to uniform pressure; thus the gravitation of the liquid is used to best advantage, just as in the case of the rubber tube recommended in the pharmacopœial directions for percolation. The body of the percolator may be made of glass or stoneware, and the evaporation of menstruum prevented by a tightly fitting cover of sheet rubber about ¼ or ½ inch thick.

Much has been written about "pressure percolators," the chief claim advanced for their use being the complete extraction of drugs with less menstruum than by ordinary methods, which applies to the preparation of concentrated solutions, such as fluid extracts. The idea of more complete solution by means of pressure originated with Count Real about 1815, and the apparatus devised by him (see Fig. 108) bears a close resemblance to some of the pressure percolators of the present day, devised by Rosenwasser, Berry, Suit, and Anderson. In the more recent apparatus the drug to be extracted is confined, by means of a suitable screw arrangement, between perforated disks, in any desired space, without the possibility of expansion on coming in contact with the

FIG. 108.



The "Count Real" pressure percolator.

bulk of the menstruum. The solvent is forced through the mass by pressure obtained from a column of liquid 10 or 12 feet in height, supplied by a reservoir.

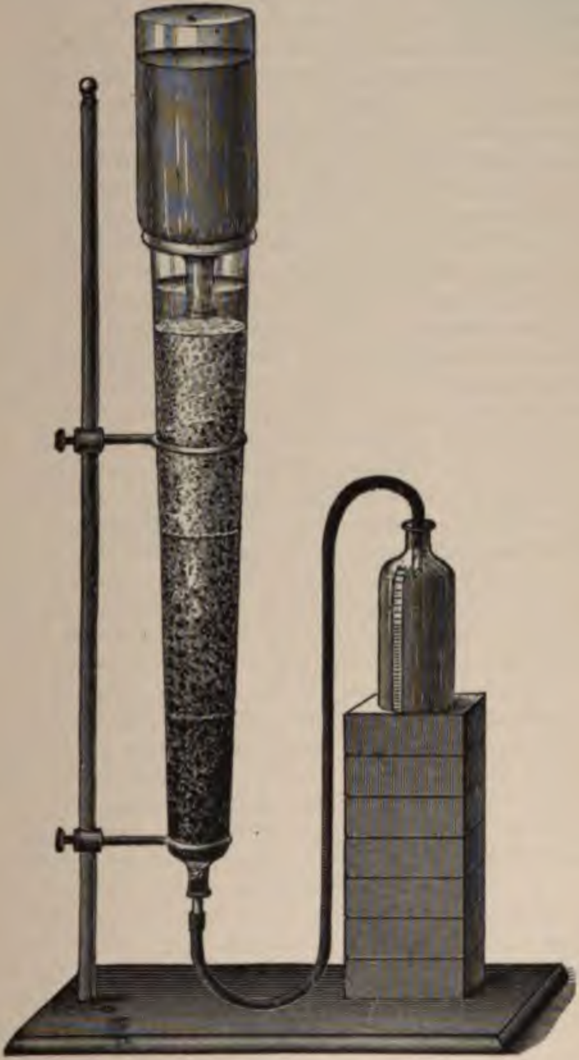
Management of the Process of Percolation.—The Pharmacopœia gives the following directions for conducting percolation, which are applicable to all official preparations in which this method of solution is indicated, as in each individual case the fineness of powder, the quantity of menstruum to be used for moistening the drug, and the degree of firmness with which it is to be packed are specified:

"The percolator most suitable for the quantities contemplated by the Pharmacopœia should be nearly cylindrical or slightly conical, with a funnel-shaped termination at the smaller end. The neck of this funnel end should be rather short, and should gradually and regularly become narrower toward the orifice, so that a perforated cork, bearing a short glass tube, may be tightly wedged into it from within until the end of the cork is flush with its outer edge. The glass tube, which must not protrude above the inner surface of the cork, should extend from 3 to 4 Cm. beyond the outer surface of the cork, and should be provided with a closely fitting rubber tube, at least one-fourth longer than the percolator itself, and ending in another short glass tube, whereby the rubber tube may be so suspended that its orifice shall be above the surface of the menstruum in the percolator, a rubber band holding it in position.

"The percolator is prepared for percolation by gently pressing a small tuft of cotton into the space of the neck above the cork, and this may then be moistened by pouring a few drops of the menstruum upon the cotton, to facilitate the passage of the first portion of the percolate, which is often very dense.

"The powdered substance to be percolated (which must be uniformly of the fineness directed in the formula, and should be perfectly air-dry before it is weighed) is put into a basin, the specified quantity of menstruum is poured on, and it is thoroughly stirred with a spatula or other suitable instrument until it appears uniformly moistened. . The moist powder is then passed through a coarse sieve —No. 40 powders and those which are finer requiring a No. 20 sieve, while No. 30 powders require a No. 15 sieve for this purpose. Powders of a less degree of fineness usually do not require this additional treatment after the moistening. The moist powder is now transferred to a sheet of thick paper and the whole quantity poured from it into the percolator. It is then shaken down lightly and allowed to remain in that condition for a period varying from fifteen minutes to several hours, unless otherwise directed; after which the powder is pressed by the aid of a plunger of suitable dimensions, more or less firmly in proportion to the character of the powdered substance and the alcoholic strength of the menstruum; strongly alcoholic menstrua, as a rule, permitting firmer packing of the powder than those weaker. The percolator is now placed in position for percolation, and the rubber tube having been fastened at a suitable height, the surface of the powder is covered by an accurately fitting disk of filtering-paper or other suitable material, and a sufficient quantity of the menstruum poured on through a funnel reaching nearly to the surface of the paper. If these conditions are accurately observed, the menstruum will penetrate the powder equally until it passes into the rubber tube, and reaches in this a height corresponding to its level in the percolator, which is now closely covered to

FIG. 109.



prevent evaporation. The apparatus is then allowed to stand at rest for the time specified in the formula.

"To begin percolation, the rubber tube is lowered and its glass end introduced into the neck of a bottle previously marked for the quantity of liquid to be received, if the percolate is to be measured, or of a tared bottle if the percolate is to be weighed; and by raising or lowering this recipient the rapidity of percolation may be increased or lessened, as may be desired. A layer of menstruum must constantly be maintained above the powder, so as to prevent the access of air to its interstices, until all has been added or the requisite quantity of percolate has been obtained. This is conveniently accomplished, if the space above the powder will admit of it, by inverting a bottle containing the entire quantity of menstruum over the percolator in such a manner that its mouth may dip beneath the surface of the liquid, the bottle being of such a shape that its shoulder will serve as a cover for the percolator. (For illustration of the official process, see Fig. 109.)

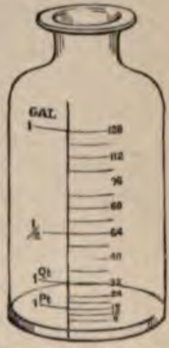
"It is obvious that the success of the process of percolation largely depends upon the regulation of the flow of the percolate; if this should be too rapid, incomplete exhaustion will result; but if too slow, valuable time may be wasted. The rate of flow for extracts and fluidextracts for 1000 Gm. of powder should range from 2 to 5 drops a minute; for official quantities of tinctures and preparations of about the same strength from 8 to 15 drops a minute; it is evident that the proper rate of flow should vary with the quantity and character of the drug employed and the density of the menstruum."

The degree of fineness of powder to which a drug is to be reduced depends partly upon the menstruum to be used and partly upon the nature of the active constituents of the drug and the readiness with which these can be extracted. Drugs like aconite, cinchona, nux vomica, veratrum viride, and others, require to be in fine powder; while gentian, rhubarb, krameria, squill, and the like, can be readily exhausted in coarser powder. As a rule, strongly alcoholic or ethereal menstrua are used with fine powders, whereas hydro-alcoholic and aqueous menstrua are better adapted to coarser powders.

The quantity of menstruum to be used for moistening the powder also varies with different drugs; one-fourth to one-half as much menstruum as powder is generally required to dampen it thoroughly without destroying its mobility, depending likewise upon the nature of the drug and menstruum. In a few cases, where the active constituents are quickly extracted, and previous moistening might cause the powder to agglutinate, as in the case of the official oleoresins, it is even better not to moisten the drug at all before placing it in the percolator.

The next step is the proper packing of the percolator, and upon it will largely depend the success of the process. A suitable support must be provided for the moistened powder, and for this purpose a notched cork or a tuft of absorbent cotton may be used. If cork be chosen, a layer of cotton should be placed over it to prevent the escape of powder; or if cotton alone be used, it may be slightly compressed into the neck of the percolator. Unless the quantity of drug be large, the moistened powder, after having been first passed through a coarse sieve to break up any lumps, should be transferred to the percolator *all at one time*, and then shaken down by tapping the sides of the vessel. If the drug is to be saturated with menstruum before maceration, as in the case of fluid extracts, the powder should be at once compressed, moderately or firmly, as the character of the menstruum and the nature of the drug may require. As a rule, fine powders and alcoholic menstrua demand firm packing, as also ligneous and spongy drugs under certain conditions; aqueous menstrua generally necessitate moderate compression. If the moistened drug be introduced in layers, uniform packing becomes more difficult; the lower portions of the drug should be less firmly compressed than the upper layers, because the menstruum, when it reaches them, being already charged with some soluble matter, is denser than at the top, and hence cannot penetrate a firmly packed mass as readily as would fresh menstruum. Maceration of the moistened powder prior to percolation is advantageous in many cases, as it allows the drug to swell and become more thoroughly permeated by the menstruum, and permits more satisfactory packing afterward; in some cases, where concentrated solutions are desired, maceration after saturation is positively necessary to insure good results. The packing of the moistened powder is best effected with a packing stick of suitable design, made of hard wood, of the shape of the well-known potato-masher. Next to uniformity in fineness of powder, uniformity in packing is the most important feature in percolation, so as to insure the even descent of the menstruum; if the drug is more firmly compressed on one side than on the other, the menstruum is sure to flow in the direction of least resistance, and leave a part of the mass imperfectly extracted. After the powder has been packed, a diaphragm of filtering paper or felt is laid over the surface and kept in place by means of pebbles or pieces of broken glass; this is for the purpose of preventing disturbance of the upper layer and to insure equal distribution of the liquid when the menstruum is poured on.

FIG. 110.



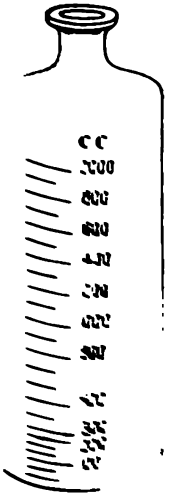
Glass receiving jar, graduated in U.S. fluid measure.

As stated in the pharmacopœial directions, a layer of menstruum must constantly be maintained above the powder, in order to prevent access of air to its interstices. Every percolator should be provided with a cover, which may be either of glass or sheet-rubber, to avoid loss of or change in the menstruum.

The simplest arrangement for controlling the rate of flow of the percolate is by means of a rubber tube, as described in the official directions, and this device can be attached to nearly every form of percolator known. As the rate of flow from the tube will be proportionate to the difference in height between the liquid in the percolator and the point to which the tube is raised on the outside, it is evident that its control is within easy reach, and may be varied from a constant stream to 2 drops per minute. The rapidity with which the percolate shall be allowed to pass will vary with the object in view and the ease with which the active principles enter into solution; for tinctures, the average rate may be stated [illegible] drops per minute, while the percolate in the case of fluid-extracts should not be allowed to flow faster than from 2 to 5 drops per minute.

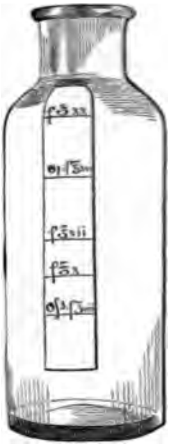
The complete exhaustion of a drug can only be judged by the physical properties of the last portions of the percolate; hence a thorough knowledge of the valuable constituents sought to be extracted is essential; absence of color and odor is not always indicative of perfect exhaustion, and the sense of taste furnishes a more reliable test in the case of aconite, ginger, nux vomica, etc. Drugs like jalap and podophyllum are known to be exhausted when the percolate mixes clear with water, as this will not occur until all resin has been extracted. Cardamom, valerian, vanilla and similar

Fig. 111.



[illegible]

Fig. 112.



Graduated glass receiving jar, home made.

[illegible] judged [illegible] by the odor of the percolate; [illegible] bitter taste; and rhatany, [illegible] astringency of their soluble [illegible]

[illegible] menstruum is sometimes

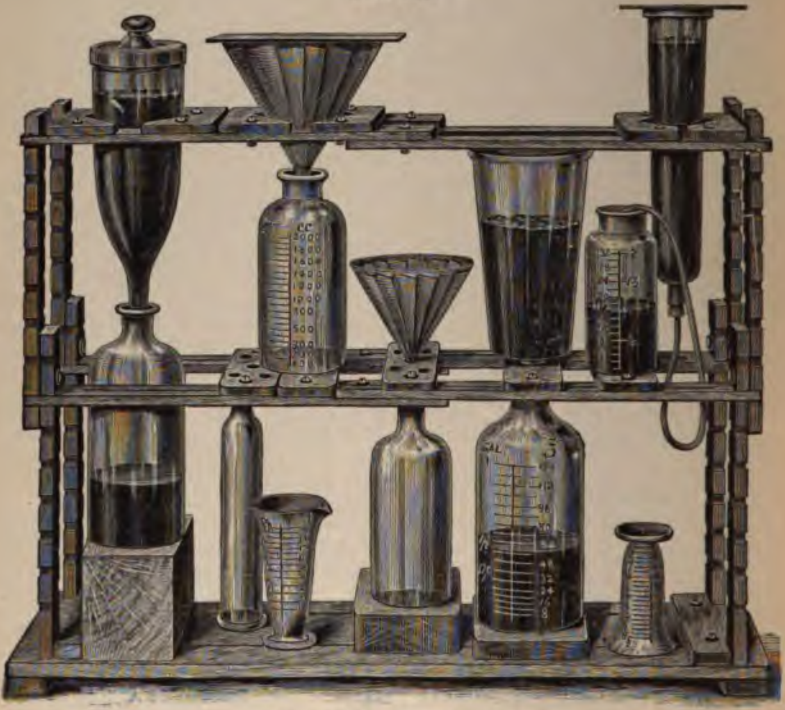
retained by the marc after exhaustion of the drug, and this may be recovered by expression or by percolation with water, either direct or after admixture with clean sawdust. Such recovered alcohol is unfit for further use until it has been purified by adding 3 grains of potassium permanganate to every pint, shaking the mixture occasionally during several days, and then decanting and distilling. Another plan to avoid the loss of alcohol by absorption is to employ gradually weaker menstrua, after the required quantity of original menstruum has all been added.

Much time and annoyance may be saved by collecting the percolate in properly graduated glass jars (if the percolate is to be weighed, use tared vessels), which can be obtained from glass manufacturers in different sizes adjusted both for apothecaries' and metric fluid measure (see Figs. 110 and 111). A convenient plan also is to paste a strip of paper on a wide-mouth bottle and mark on the same with ink the different quantities of liquid measured into the bottle, as shown in Fig. 112; to protect the paper scale and render it impervious to moisture, it should be coated with colorless varnish.

The usual method of supporting percolators is by means of the iron rings of a retort-stand, as shown in Fig. 109; in order to protect the glass, sections of rubber tubing may be attached to the rings, forming suitable cushions or guards. A very convenient arrangement is Beck's percolating stand (see Fig. 113), which admits of simultaneous multiple operations and is equally well adapted for use in the store or laboratory. The stand can either be placed on the floor or be supported on two iron brackets fastened to the wall; as shown in the illustration, it can be changed by means of thumb-screws to suit various heights of bottles. The length of the base-board is 42 inches, the width 12 inches, and the extreme height of the stand 36 inches; the supports for percolators and funnels are formed by means of cross-pieces suitably hollowed out and secured by screws passing through the slot in the cross-bars.

Repercolation is a process intended for the preparation of concentrated vegetable solutions with a minimum quantity of menstruum, and is confined to the manufacture of fluid extracts without heat. Dr. Squibb, who was the author of the process, defined it to be "the successive application of the same percolating menstruum to fresh portions of the substance to be percolated." His suggestion was based upon the observation that a weak solution of the constituents of a drug is a better solvent for the soluble active principles of that drug than fresh menstruum. The following example will serve to illustrate the process of repercolation: 1000 Gm. of a properly powdered drug are divided into five portions of 200 Gm. each; one portion is moistened, packed, macerated, and percolated to exhaustion, the first 150 Cc. of the percolate being set aside as finished product, the remainder being collected in fractions of 200 Cc., and numbered respectively 1, 2, 3, etc., in the order in which they are collected. The second portion of the drug is moistened with No. 1 weak percolate, packed and percolated to exhaustion, the different weak percolates being used in the order in which they have been collected, followed by fresh menstruum if necessary, the first 200 Cc. of the percolate from this second portion of the drug being set aside as finished product, the remainder being again collected in fractions of 200 Cc., and numbered 1, 2, 3, etc., as before. The third, fourth, and fifth portions of the drug are treated exactly like the second portion, the first 200 Cc. of the percolate in each instance being set aside as finished product. When the fifth portion of the drug has been exhausted there will be on hand five lots of finished product—150, 200, 200, 200, and 200 Cc.; total, 950 Cc.—and besides, four or five lots of weak percolate supposed to hold in solution the soluble matter from 50 Gm.; these weak percolates, properly numbered, are set aside, to be again used in place of fresh menstruum for the next lot of the same preparation, the process henceforth being continued exactly as directed above for the second portion of the drug. This retention

FIG. 113.



Beck's percolating stand.

of 25 per cent. of the soluble matter of one portion of the drug in the weak percolates is based on numerous carefully conducted experiments, the results of which showed that when 100 Gm. of drug are exhausted by percolation, from 70 to 80 per cent. of the total soluble constituents present are contained in the first 75 Cc. of percolate. By some the process of repercolation is termed fractional percolation, and modifications of Squibb's method, stated above, have been suggested; in every instance, however, the same principle is kept in view, namely, the use of weak percolates instead of fresh menstruum.

Continuous percolation is a name sometimes applied to a process of extraction which involves the exhaustion of a drug with a limited quantity of menstruum, by repeatedly vaporizing and condensing the fluid in a specially constructed apparatus, so arranged that the extracted soluble matter remains in the receiving flask, while the solvent, in the form of vapor, passes upward to a reflux condenser, and thence flows back into the percolator. This process is chiefly employed in the examination of vegetable drugs, with a view to determine their valuable constituents, and is particularly adapted to the manufacture of the official oleoresins. For description of the apparatus employed, see the chapter on Oleoresins.

CHAPTER IX.

SEPARATION OF NON-VOLATILE MATTER.

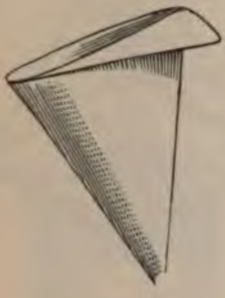
THE process of separation may be applied to non-volatile or fixed as well as volatile matter; in the former case it is understood to refer to the removal of insoluble substances, sediments, etc., from fluids holding them in suspension, and also of immiscible fluids from each other. The various operations employed for the separation of solids from fluids are termed filtration, decantation, expression, clarification, and decoloration.

FILTRATION.

By some pharmacists filtration is considered so trivial an operation as not to merit extended consideration; but, like other simple processes, it is well deserving of study, as there is room for the exercise of intelligence and ingenuity in its many useful modifications. Filtration is usually employed when the solid matter to be removed is not present in excessive quantity, and consists in submitting the mixture to the separating action of certain media which allow the fluids to pass through but are impervious to the solid particles. Sometimes filtration is also called colation or straining; but it is understood that the process of straining differs from filtration either in the less complete removal of suspended sedimentary matter from a fluid, or in the fact that the solid particles are not in fine powder and can be easily retained by coarser media than those generally employed for filtration. Colation is a favorite mode of separation when the fluid is of a viscid character. The various filtering media employed are cotton and woollen cloth, paper made therefrom, also absorbent cotton, glass wool, asbestos, sand, and charcoal; the clear liquid passing through these media is termed the filtrate.

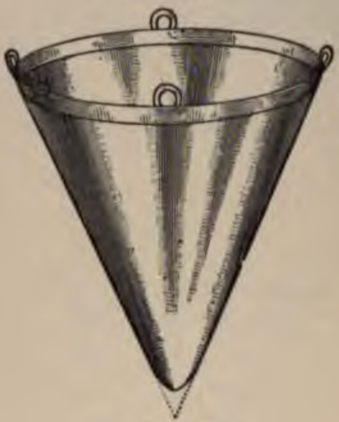
For straining syrups, oils, and similar fluids, filter-bags of flannel or felt are admirably adapted, as they permit a rapid passage of the liquid and effectually retain all solid matter; such filter-bags are of conical shape (see Figs. 114 and 115), and are readily made, of plain or Canton flannel, by folding over a square piece in the manner indicated in Fig. 116, the line *cd* being laid over the line *ca* and united by a seam; the bag thus formed is pointed at *c* and open from *a* to *b*, the line *ac* being lapped over to form the seam. The long end projecting toward the point *b* beyond the dotted line *ef* should be removed, and four loops of heavy cord or tape attached after the edge has been turned over; the loops will serve to suspend the filter-bag properly in a square or round frame, as shown in Fig. 117. For some purposes, as the straining of dense saline solutions or the washing and draining of bulky precipitates, a square cotton cloth may be stretched over a square frame called a *tenaculum*, as shown in Fig. 118; for smaller operations, such as straining infusions or decoctions, the cloth strainer may be fastened over a funnel by means of wooden pinchcocks, and when it becomes necessary to strain with expression the ends of the strainer must be folded over and twisted in opposite directions, as shown in Fig. 119. A kind of cotton cloth known as cheese-cloth is preferred by many for strainers, as it allows liquids to pass rapidly through it. All strainers should be well wetted just before they are used, and those containing sizing should be freed from the same by washing with hot water before they are put into use. For use at the dispensing counter in straining solutions, a pledget of absorbent cotton placed in the throat of a funnel will be found very convenient and serviceable; and as nearly every solution prepared is likely to contain some specks and motes, this little operation should never be neglected.

Fig. 114.



Flannel strainer.

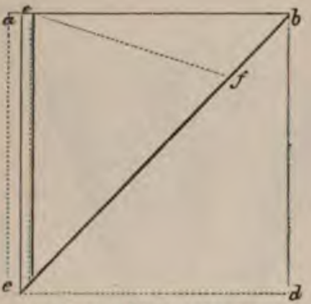
Fig. 115.



Filter-bag.

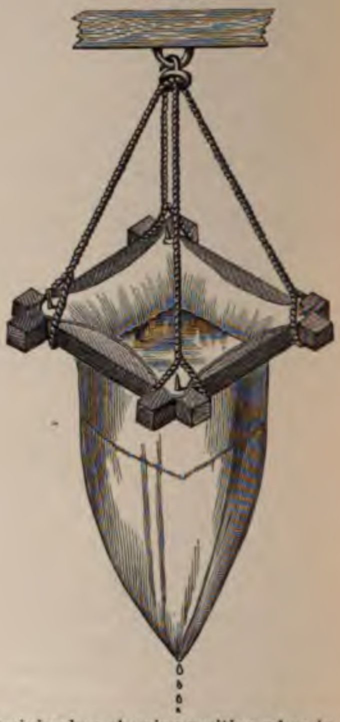
Some years ago a very serviceable oil filter was devised by William R. Warner, which possesses the advantage of filtration under pressure, and is equally well adapted to syrups (see Fig. 120). The upper cylindrical vessel of tinned iron is 22 inches high and 10 inches in diameter, with a flanch rim soldered on the bottom, of rather less diameter and 1 inch wide, so as to fit firmly into the open top of another cylindrical vessel, B, of the same diameter, 18 inches high. The upper vessel is furnished with a lid and with an L-shaped tube and stopcock, c, which penetrates the side close to the bottom, and fits into another tube, *d*, at *e*, which tube opens into the lower vessel close to its base, and is further secured to B by a tubular stay. The filtering medium is a cone of hat felt, projecting upward from near the bottom of the lower vessel, and secured in place by thumb-

FIG. 116.



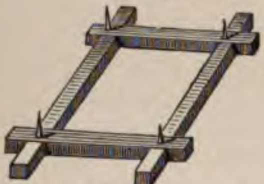
Manner of folding strainer.

FIG. 117.



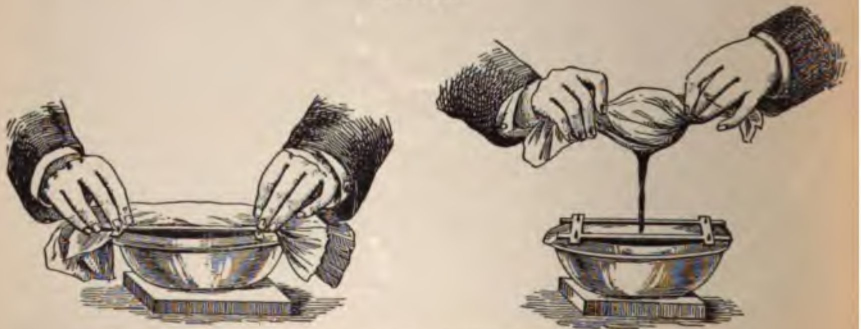
Straining-bag, showing position when in use.

FIG. 118.



Frame for cloth or flannel strainers, known as "tenaculum."

FIG. 119.

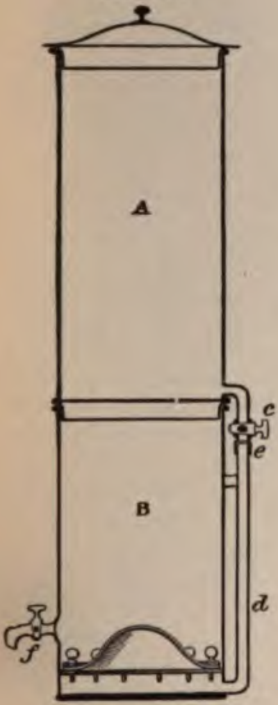


Showing the manner of folding and expressing flannel or cloth strainers.

screws passing through two tinned-iron rings and the felt, which are all properly pierced for that purpose. The stopcock *c* being closed, the upper vessel is fitted in its place, and the tube-joint *e* rendered tight by wrapping with isinglass plaster; when this is dry, the upper vessel is filled with the liquid to be filtered, and the stopcock *c* opened. The filtered liquid as it accumulates in B should be drawn off at *f*, and if convenient the apparatus should be kept in a temperature of about 50° C. (122° F.), in order to facilitate the flow of the liquid.

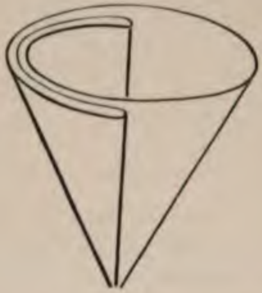
Complete separation of fine suspended matter from fluids can best be effected by means of filtration through paper; only unsized paper should be used, the best kind being that made from cotton and linen rags, although paper made from woollen material is tougher, and, being more porous, permits more rapid filtration. The square sheets of filtering paper, which at one time were the only style to be had, are rarely used now, since ready-cut round filters can be had of all sizes and qualities. Two kinds of paper filters are used, the *plain* and the *plaited*, the construction of which is very simple, and, when once properly understood, never forgotten. The chief advantages of plain filters are the simplicity of construction and the fact that they are admirably adapted for collecting the solid matter suspended in the fluid, which is afterward to be removed from the paper for further use; on the other hand, filtration proceeds far less rapidly in a plain than in a plaited filter, because the paper lies flat against the sides of the funnel, and the liquid passes through only at the point or apex. Plain filters are made by doubling a circular piece of filtering paper upon itself, and then folding this directly in

FIG. 120.



Warner's oil filter.

FIG. 121.



A plain filter.

the middle; by now opening the folds in such a manner that one sector or division shall appear on one side and three sectors on the other side, a perfect cone will be obtained, as shown in Fig. 121, which will exactly fit into a properly shaped funnel.

FIG. 122.

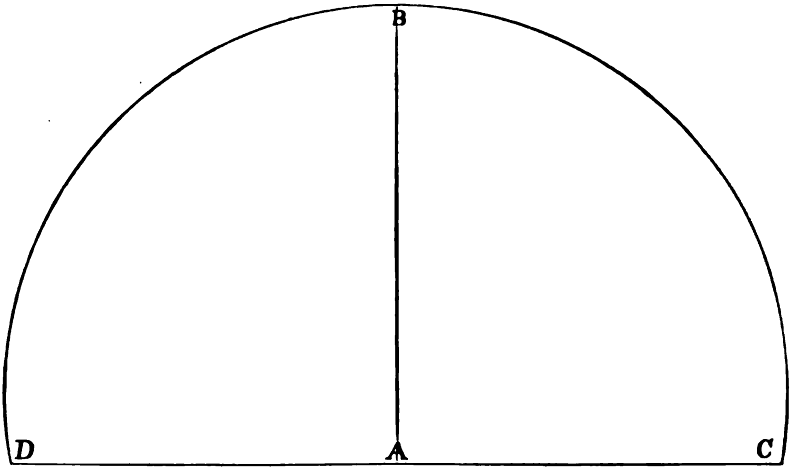
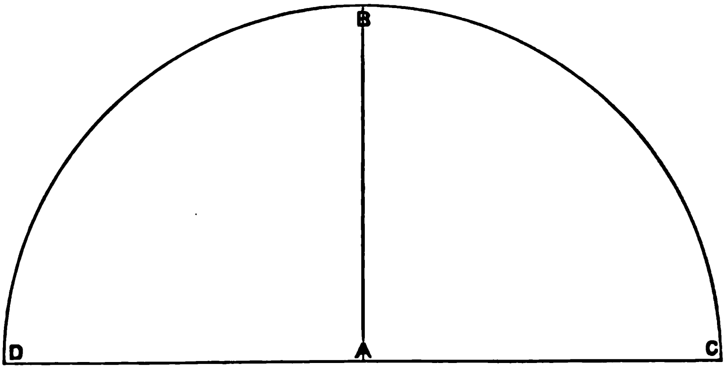


Diagram for making an economical plain filter, according to E. Classen's directions.

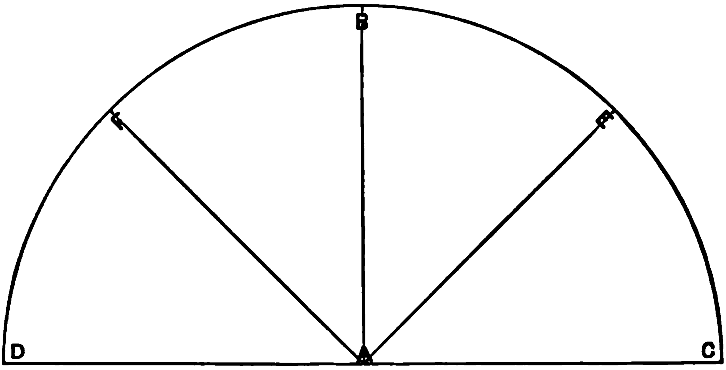
The waste of paper which is caused by this method of folding a plain filter, where three thicknesses of paper are found on one side of the filter and but one thickness on the other side, may be avoided by following the suggestions of Edo Classen, which are as follows:

FIG. 123.



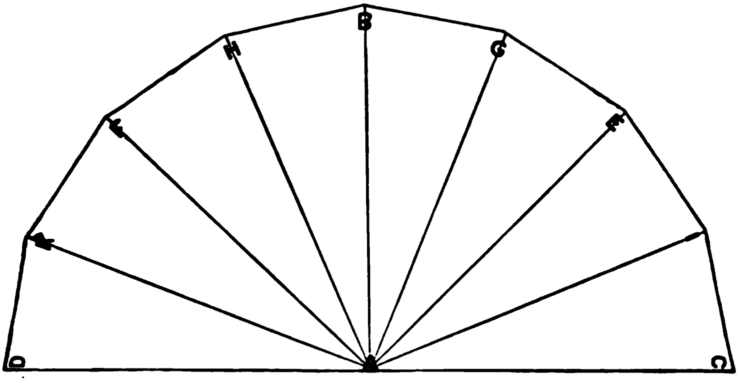
To make a plain filter, of single thickness, which will fit a funnel having an angle of 60 degrees, use a piece of filter paper in the shape of a semi-ellipse, as shown in Fig. 122, the line AB being one-fifth longer than the line AC or AD. Fold the paper in the centre so that one-half exactly covers the other; next fold the short, straight side over, so that both straight sides shall be of the same length. Additional security against leakage will be obtained if the strip last folded is again folded upon itself, preferably toward the inside.

FIG. 124.



In order to strengthen the weakest point of the cone, a smaller round filter may be placed on the outside of the larger filter and folded with the same; or one plain filter may be placed inside of another, so that even thicknesses of paper shall be on all sides.

FIG. 125.



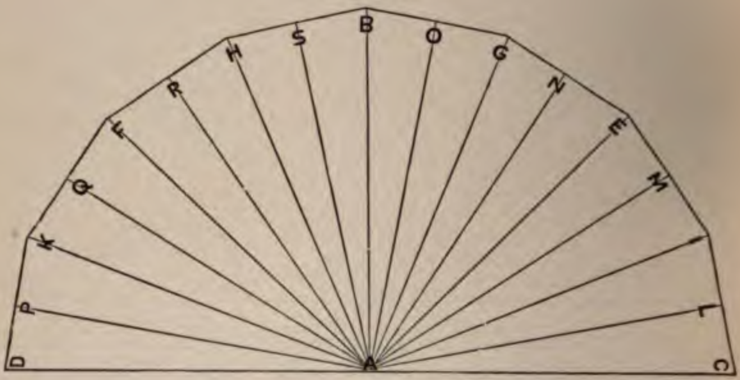
The construction of a plaited filter is more readily demonstrated than explained; the simplest plan is to proceed as follows: Fold a circular piece of filtering paper twice, after the manner directed above for a plain filter; this gives creases AB, AC, and AD (see Fig. 124).

Next fold the crease AC over on AB, and the crease AD over on AB; this causes the creases AE and AF (see Fig. 124).

Now fold the crease AC over on AF, the crease AD over on AE, the crease AC over on AE, and the crease AD over on AF; this causes the creases AG, AH, AI, and AK (see Fig. 125).

The semicircle is now divided into 8 sectors, all creases being in the same direction; to complete the filter it is necessary to divide each sector into two by making a crease in a direction opposite to those already made—thus (see Fig. 126):

FIG. 126.



Showing the creases of a plaited filter.

Fold the triangle ACI back upon itself; this causes the crease AL.
“ “ “ AIE “ “ “ “ “ “ “ AM.
“ “ “ AEG “ “ “ “ “ “ “ AN.
“ “ “ AGB “ “ “ “ “ “ “ AO.
“ “ “ ADK “ “ “ “ “ “ “ AP.
“ “ “ AKF “ “ “ “ “ “ “ AQ.
“ “ “ AFH “ “ “ “ “ “ “ AR.
“ “ “ AHB “ “ “ “ “ “ “ AS.

If the filter now be opened, it will be found divided into 32 sectors, 2 of which, ACL and ADP, opposite each other, show both edges pointing in the same direction (see Fig. 127); to prevent these 2 sectors from lying flat against the glass when the filter is placed in the funnel, they should be again divided by placing the index finger in the centre and bringing the edges up with the thumb and second finger, thus forming two new creases inward, AU and AV (see Fig. 128). In plaiting a filter, care must be observed that the creases be not pressed too firmly down to the very point, as this has a tendency to rupture the paper, or at least to weaken it materially. The plaited filter, when completed and ready for use, is divided into 34 sectors, and appears as shown in Fig. 129.

The points of paper filters may be toughened or strengthened by dipping them into strong nitric acid of 1.42 sp. gr., and then washing well with water to remove excess of acid; while a similar treatment with sulphuric acid converts unsized paper into parchment paper, which is impervious to water. Nitric acid simply toughens the paper, but in no wise interferes with the absorption and passage of fluids through it, though its power of resistance is increased tenfold by this treatment.

FIG. 127.

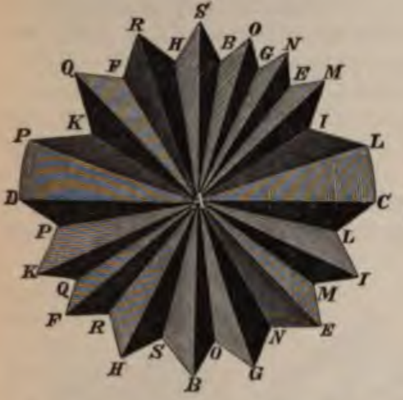
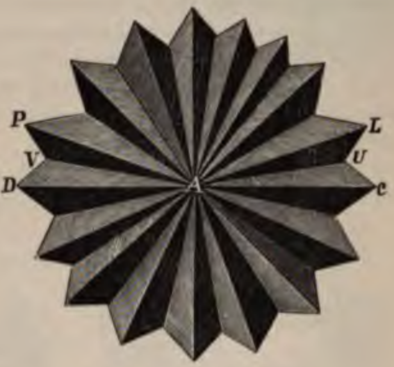
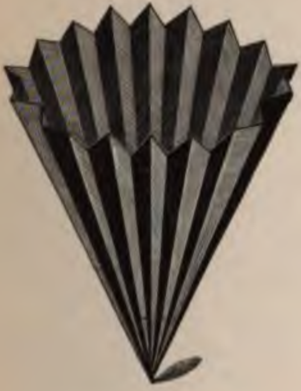


FIG. 128.



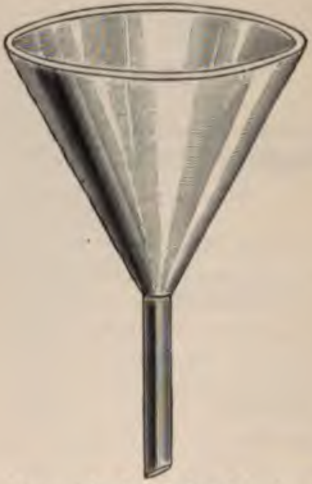
When the object of filtration is to obtain a clear fluid irrespective of the solid matter removed, a plaited filter is always to be preferred to a plain one, as it exposes the entire surface of the paper to the liquid and allows the latter to pass through very rapidly.

FIG. 129.



A complete plaited filter.

FIG. 130.

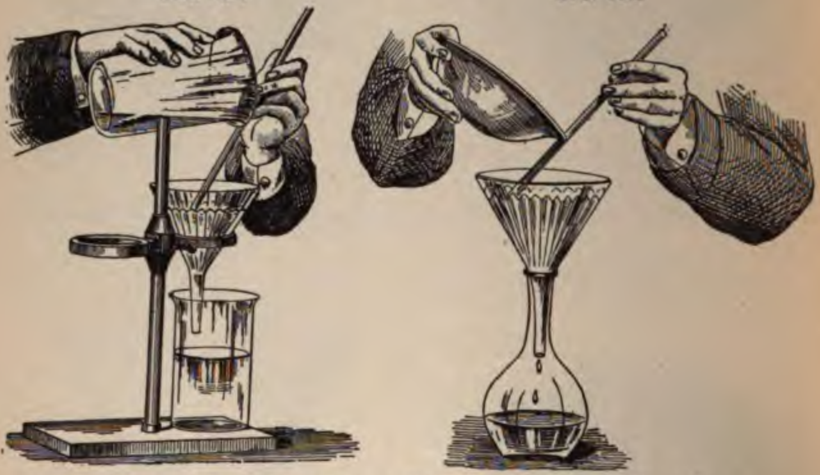


A properly shaped glass funnel.

Glass, porcelain, or metallic funnels, intended as supports for paper filters, should be of the shape shown in Fig. 130, having straight sides at an angle of 60 degrees to each other, and the end of the tube being cut off obliquely, so as to compel the liquid to flow from one point only; when used over a jar or beaker it is well to place the lower end of the funnel in contact with the side of the vessel, thus preventing any annoyance from splashing of the liquid. In order to provide for the necessary escape of air from the receiving vessel, whenever a funnel is placed in a bottle a piece of twine or a strip of paper should be placed between the neck of the bottle and the tube of the funnel, the end of which should invariably project below the neck of the bottle.

When a paper filter is placed in a funnel, its upper edges should never quite reach to the rim of the funnel (better ½ inch below), so as to allow the funnel to be covered with glass or sheet-rubber, for the purpose of keeping out dust and preventing evaporation; besides, if the filter projects beyond the funnel, considerable liquid will be drawn to the upper edges, owing to the capillarity of the paper, and evaporated, thus entailing a loss. In pouring a liquid into a filter, it should never be allowed to fall in a stream upon the apex or point, which is likely to break from the sudden force, but should be directed against the side by means of a guiding-rod, as shown in Figs. 131 and 132.

Fig. 131. Fig. 132.

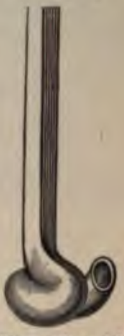


Manner of pouring liquids into a filter with the aid of a guiding-rod.

To insure a continuous supply of liquid to the filter, a bottle containing the fluid may be inverted over the funnel in the manner shown in Fig. 109, for supplying menstruum to a percolator.

For filtration of very volatile liquids, a glass tube, bent as in Fig. 133, may be placed under the filter against the side of the funnel; the twisted end will prevent the tube from slipping down, and air from the receiving-bottle can readily pass up through the tube, which should reach a little above the paper filter. The funnel, which should pass air-tight through a cork, must also be closed hermetically at the top.

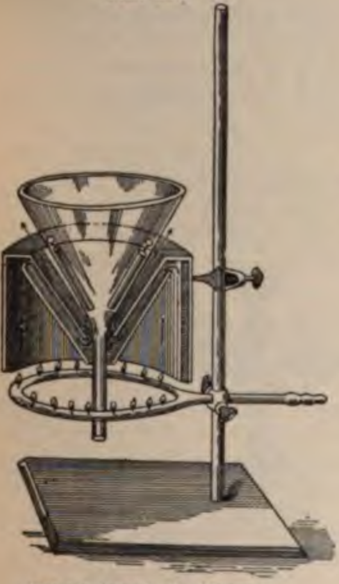
Fig. 133.



Glass tube with twisted end.

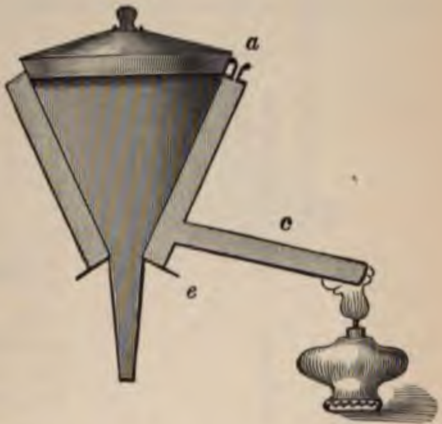
Occasionally the filtration of substances which are not fluid at ordinary temperature becomes necessary, such as mutton suet, wax, petrolatum, ointments, etc.; this can be effected either by means of a hot-air funnel or a water-bath funnel. When hot air is to be used, the funnel containing a filter is suspended by means of porcelain strips, in a heavy tin jacket, which is surrounded by a copper cylinder, and heat is supplied from a circular low-power burner, as shown in Fig. 134, the heated air continually circulating around the funnel. The water-bath funnel consists of a glass funnel surrounded by a double tin or copper jacket, as shown in Fig. 135; the opening, *a*, at the top of the jacket is for the purpose of introducing hot water, and the projecting tube, *c*, near the bottom, for maintaining the heat of the water by means of a spirit lamp or gas jet. The projecting rim, *e*, is intended to prevent any water, running over at *a*, from entering the bottle or vessel, in the mouth of which the neck of the funnel may be placed. The substance to be filtered should first be

Fig. 134.



Hot-air funnel. (L. Meyer.)

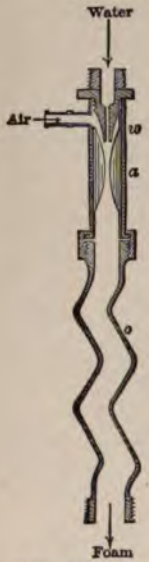
Fig. 135.



Sectional view of hot-water funnel with cover.

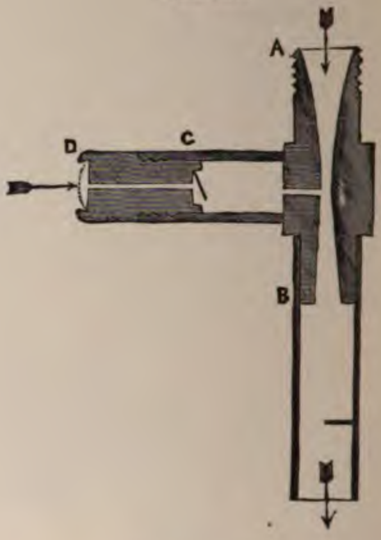
completely melted and then poured into the filter contained in the previously heated funnel, which must be kept covered to avoid loss of heat.

Fig. 136.



Richard's filter pump.

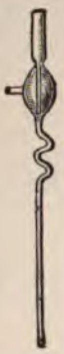
Fig. 137.



Chapman's filter pump.

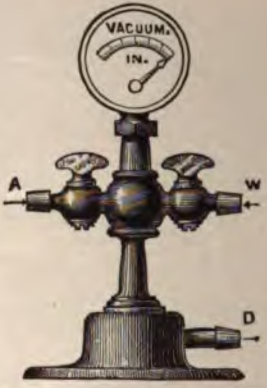
The rate of filtration of a liquid can be greatly increased by exhausting the air from the funnel-tube and receiving-bottle, thereby increasing the atmospheric pressure above the liquid ; the necessity for this operation occurs more frequently in the analyst's laboratory than with pharmacists, yet an acquaintance with the apparatus employed

Fig. 138.



Geissler's glass filter pump.

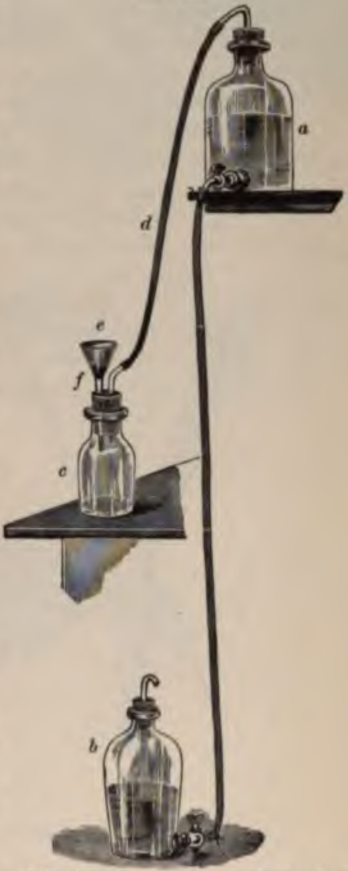
Fig. 139.



Portable filter pump, with manometer.

is desirable. The exhaustion of the air is effected by means of an aspirator connected with a water-supply and with the receiving-bottle by rubber tubing. Figs. 136, 137, 138, and 139 represent different styles of filter pumps; as seen in two of the illustrations, suction of air is produced by forcing water, under pressure, through a contracted space which communicates with the air to be aspirated. The internal construction of the pump shown in Fig. 139 is similar to that of the other two, but the water which enters at W is discharged at D on the side; hence this apparatus can be used at any desired point, being connected by means of tubing with the water-supply and sink: with air-tight connections a nearly absolute vacuum can be obtained, as may be seen from the indications of the manometer attached to the top of the pump. Whenever filter pumps are used, the pressure on the liquid filtering becomes so great as to endanger the safety of the filter point; an extra support is therefore provided in the shape of a finely perforated platinum cone set in the throat of the funnel in which the paper cone is placed.

FIG. 140.



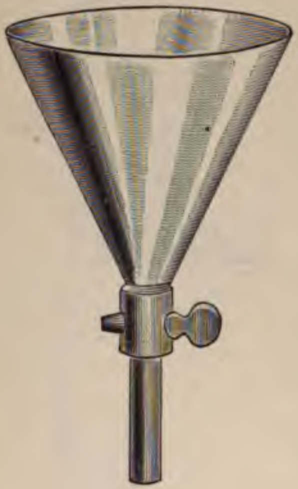
Filtering apparatus. *a* and *b* are two large bottles connected, as indicated in the drawing, by a narrow India-rubber tube with thick walls. The upper bottle should be placed as high as possible. *c* is a bottle into which the filtrate is to pass. The interior of this is in connection with *a* by a thick-walled tube, *d*. Into the stopper of *c* the funnel *e* is fixed, and at its apex lies a small perforated platinum cone, *f*, which supports the apex of the filter when the interior of *c* is partially exhausted by the discharge of the water in *a* into *b*.

When an aspirator or filter pump is used in connection with water drawn from the city supply, a very annoying accident sometimes happens when the water pressure is suddenly reduced, or when the pump is cut off, namely, a portion of water is drawn up into the vessel from which the air is being aspirated; this can be guarded against by interposing another vessel between the pump and the aspirated vessel.

For rarefying the air under filters when water pressure is not available, a simpler contrivance may be resorted to, as shown in Fig. 140; the water flowing from the upper to the lower bottle withdraws air from the receiving-flask, and by simply changing the bottles when the upper one becomes empty the operation may be continued for any length of time, the air-tube being closed by means of a pinchcock while the bottles are being changed. Ordinary 5-gallon castor-oil cans may be conveniently used in place of bottles.

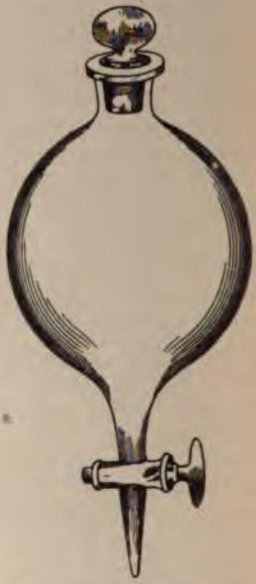
The turbidity of some liquids is caused by suspension of matter in so finely divided a form that its removal cannot be effected by the ordinary methods of filtration, and recourse must be had to the interposition of some other substance to render the liquid perfectly transparent and clear; in such cases paper pulp, calcium phosphate, and purified talcum form excellent filtering media.

Fig. 141.



Glass separator (funnel shape).

Fig. 142.



Glass separator (globe shape).

Paper pulp is readily prepared from scraps of filtering paper by treating them with hot water in a mortar or with active agitation in a bottle. When the paper has become thoroughly pulped the excessive moisture may be removed by expression in a clean cloth, after which the pulp may be added to the liquid to be filtered and thoroughly incorporated by agitation. The finely divided pulp forms a layer on the surface of the filter which effectually prevents the passage of minute particles of insoluble matter by absorbing these into its own fibre. For acid liquids, finely shredded asbestos is preferable.

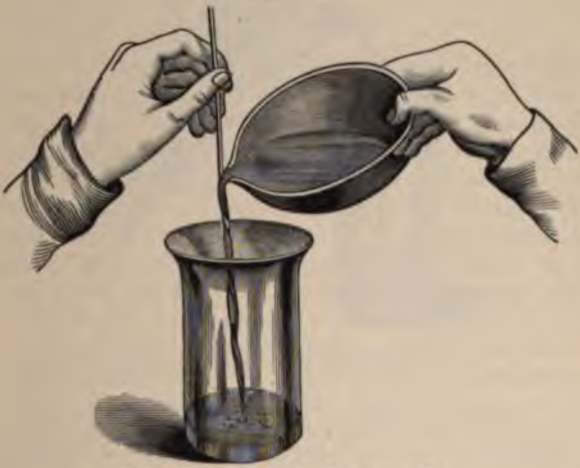
Immiscible liquids can be conveniently separated from each other by pouring the mixture into specially constructed apparatus known as separators or separatory funnels (see Figs. 141 and 142), and after the liquids have separated into distinct layers by reason of their different specific gravities, withdrawing the lower liquid by carefully opening the stopcock in the tube and allowing it to flow into a suitable receiving vessel.

DECANTATION.

Decantation, or the process of pouring a fluid gently from one vessel to another, is employed in pharmacy more particularly in connection with the washing of precipitates; sometimes it is resorted to for the separation of immiscible liquids, but separation in such a case can never be so complete as by the method explained above.

All precipitates when freshly obtained by double decomposition of two soluble substances, are more or less contaminated with a solution of the other newly formed salt; to remove such impurities the process of washing, which consists in treating the precipitate repeatedly with fresh portions of water, is employed. Thus, when solutions of lead nitrate and potassium iodide are mixed, the newly formed lead iodide is deposited, while potassium nitrate remains in solution, and must be removed before the precipitate can be dried. The thorough washing of precipitates is a very important operation, which may be performed by continued treatment with water on filters and cloth strainers, or by allowing the liquid in which the precipitate was formed to settle completely in suitable vessels, decanting the clear supernatant fluid, adding successive portions of fresh water, and again decanting after each settlement; it is essential that the fresh water and precipitate be well mixed by stirring or agitation after each addition.

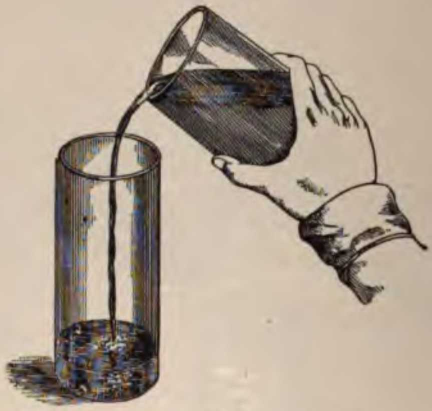
FIG. 143.



Decantation with aid of a glass rod.

The decantation of a fluid is not always so simple an operation as it may seem; the shape and size of the vessel from which the liquid is to be poured, the nature of the liquid and the height to which it fills the vessel, all influence the flow of the liquid. When the fluid to be decanted is water or an aqueous solution, and the vessel is not very large, either with or without a lip, the simplest plan is to transfer the liquid with the aid of a glass rod, as shown in Fig. 143. The guiding-rod prevents the splitting of the current of the liquid, to which is due the well-known phenomenon of liquids running back on the sides of the vessel from which they are poured. When the vessel from which the liquid is to be poured is too large or too full of liquid to admit of decantation with the aid of a glass rod, the liquid may be made to flow in a somewhat contracted but solid stream by greasing the rim of the vessel with a little resin cerate, which prevents adhesion of the liquid to the glass and enables the force of cohesion to keep the particles of liquid united; Fig. 144 illustrates the operation.

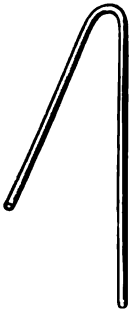
FIG. 144.



Decantation with aid of a greased rim.

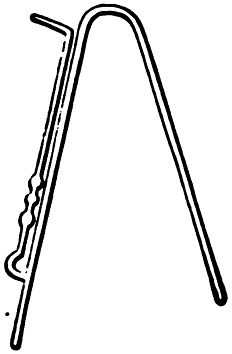
Sometimes an instrument called a *siphon* is employed to draw off the supernatant liquid from a precipitate, the method being particularly desirable if the precipitate is light and easily disturbed by handling the vessel; the simple construction of a siphon is shown in Figs. 145 and 146. The two limbs of the glass tube are of unequal length, the shorter one being immersed in the liquid; it is manifest that if the air be entirely withdrawn from the tube by suction, the liquid will rise and fill the tube, owing to the pressure of the atmosphere on the surface of the liquid. The flow of the liquid, having been started, will continue by reason of its downward tendency or gravitation aided by atmospheric pressure, until the liquid falls below the mouth of the shorter limb, or until it rises in the receiving vessel to the level of the liquid in the vessel from which it flows. A plain rubber tube may often be used with advantage as a siphon, remembering that the end of the tubing out of the liquid should always reach lower than that in the liquid, so as to insure a continuous flow.

FIG. 145.



Plain siphon.

FIG. 146.



Glass siphon with lateral suction tube.

CLARIFICATION.

Clarification is a process of separation designed to render cloudy or turbid liquids transparent by means other than those thus far considered; it is generally effected through the agency of heat; in every instance, however, the separated disturbing element must subsequently be removed by filtration or decantation. The viscid character of some liquids renders the various methods of filtration impracticable; whereas the mere application of heat, by increasing their fluidity, enables the suspended particles of solid matter to separate spontaneously, some rising to the surface while others sink to the bottom; if the liquid be allowed to remain at perfect rest while separation is going on, the lighter particles will form a layer, which can often be completely removed with the aid of a skimmer, while the heavy sedimentary matter is readily retained on a cloth strainer. Honey and balsam of fir may be treated in this manner. Saline solutions concentrated for the purpose of crystallization are frequently contaminated with dust and other foreign matter which passes freely through cloth and paper filters; they may be readily clarified by adding paper pulp (see page 158), which effectually removes the fine particles of dirt from the boiling liquid, by enveloping them in its own fibre and retaining them on the strainer.

Other substances added to turbid liquids in order to effect clarification are egg-albumen, gelatin, and milk. White of egg, or albumen, possesses the property of coagulating or solidifying when heated to about 80° C. (176° F.), therefore when it is added to liquids and then heated, any solid matter impairing the transparency of the liquids will be enclosed in the coagulum formed, and can then be removed by straining; some vegetable solutions prepared with cold aqueous menstrua contain albuminous matter originally present in the drug, which, upon heating to the boiling-point, is coagulated, and is thus gotten rid of, as in the case of extract of gentian. Albumen is preferably mixed with a little water before adding it to the liquid to be clarified, and then thoroughly incorporated with it before heating. Since albumen forms insoluble compounds with some plant constituents, it must be judiciously employed, lest the active principles contained in a liquid be removed by it. When the turbidity of a liquid is due to tannin, gelatin is generally preferred as a clarifying agent; it is used like albumen, and forms insoluble tannate of gelatin, or leather. Milk is especially adapted to clarifying acid liquids, as the casein of the milk is coagulated by the acid, and thus the impurities are removed by becoming enveloped in the coagulum.

Clarification of liquids may also be effected by subsidence and fermentation; the former is often applied to fixed oils, which are allowed to remain undisturbed in tightly closed containers for some time, so that albuminous matter derived from the seed may gradually separate and settle to the bottom. Fruit juices, as a rule, contain certain principles which tend to render them cloudy and unsightly, but which can be removed by fermentation at a moderate temperature, about 20° C. (68° F.); the matter thus separated settles to the bottom and the clear liquid may be drawn off by means of a siphon or otherwise.

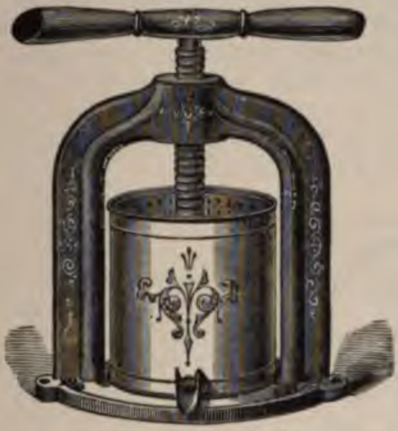
DECOLORATION.

Decoloration, as the name indicates, is a process for the removal of color from liquids, and is practised on a large scale in sugar refineries. For pharmaceutical purposes it is chiefly confined to solutions of organic acids, alkaloids, and neutral principles. The most effective decolorizing agent is animal charcoal, made either from bone or blood; ordinary bone-black requires purification by means of hot hydrochloric acid, whereby certain lime-salts are removed. Animal charcoal is preferably used in a granular condition, and its utility as a decolorizer depends upon its porosity; unfortunately, charcoal absorbs also other matters held in solution besides color, and this may occasion loss of valuable constituents unless the charcoal is subsequently washed with fresh menstruum. The usual method of employing animal charcoal is either by digesting it with the liquid to be decolorized, or by allowing the latter to percolate slowly through a column of the charcoal; in the former case the liquid requires subsequent filtration.

EXPRESSION.

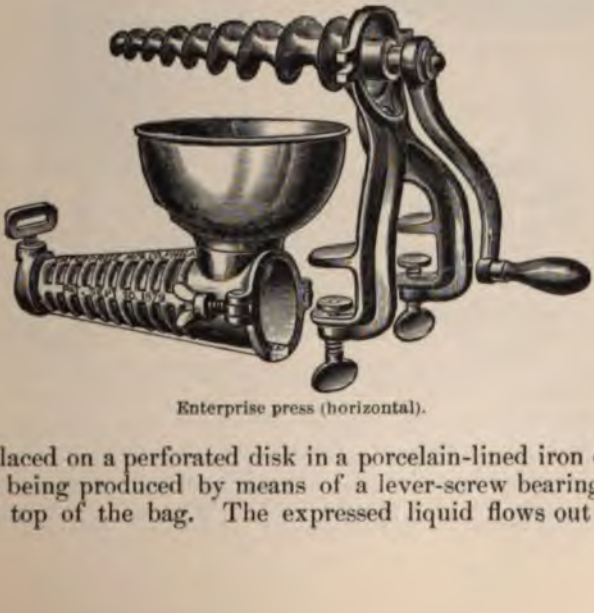
Expression is a process of separation which requires the exercise of more or less force, since it is employed in those cases where the amount of liquid is small compared with the quantity of solid matter to be removed; as, for instance, in the preparation of fruit juices, the expression of macerated drugs, or the recovery of menstruum that may have been retained by the marc in percolation when water fails to force it through. For the purposes of the pharmacist, the tincture press, Fig. 147, and the Enterprise press, Fig. 148, will be found very serviceable; in the former the substance to be expressed, having been put into a suitable canvas or press-cloth bag, is placed on a perforated disk in a porcelain-lined iron cylinder, pressure being produced by means of a lever-screw bearing upon a plate on top of the bag. The expressed liquid flows out through

FIG. 147.



Tincture press (vertical).

FIG. 148.

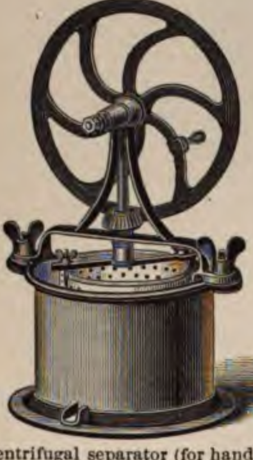


Enterprise press (horizontal).

the lip attached to the cylinder. The Enterprise press is operated without the use of press-cloths, the material to be expressed being fed directly into the hopper communicating with a tapering cylinder containing a large screw, the thread of which gradually diminishes in size toward the smaller end; the cylinder is provided with a perforated plate in the bottom, and the material is compressed by means of the tapering screw, which is turned with a crank. The dry residue is discharged through an opening in the small end of the cylinder, and the liquid expressed flows out through the perforated plate.

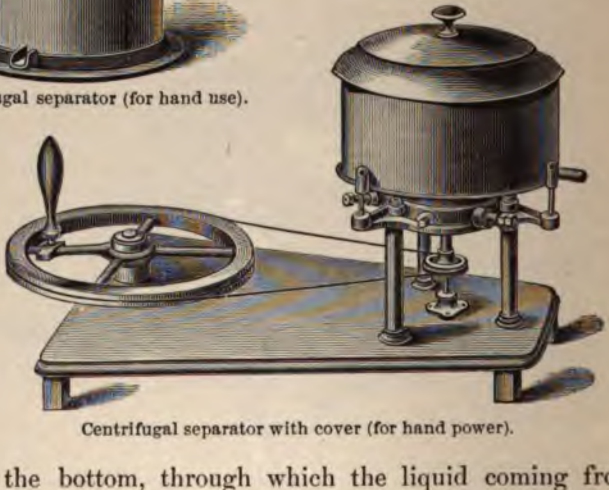
Another method of separation is that effected by means of centrifugal machines, which are extensively employed in manufacturing establishments for washing and drying crystals as well as for the rapid withdrawal of moisture in the drying of certain precipitates and fabrics. The apparatus used consists of a metal drum or cylinder having a solid bottom but open at the top, and provided with perforated sides, which revolves on its own axis inside of a larger stationary cylinder supplied with a cover to keep out dust, and an outlet tube at the bottom, through which the liquid coming from the inner cylinder is allowed to flow out; sometimes the perforated sides of the inner cylinder are covered with bolting-cloth, according to the substance to be operated upon, and the rotary motion is

FIG. 149.



Centrifugal separator (for hand use).

FIG. 150.



Centrifugal separator with cover (for hand power).

imparted to the cylinder from below by means of steam power. The value of centrifugal machines depends upon the velocity with which the material to be centrifugalized is hurled around and against the perforated sides, the revolutions usually numbering as high as 2000 or 3000 and even more per minute; the strong draft of air created between the walls of the inner and outer cylinders by such rapid revolution effects drying of the material more thoroughly than is possible by expression or other means. The use of centrifugal machines is based on the well-known laws of motion and inertia, according to which a body put in motion continues in a straight line unless turned from its path by some external force, and thus liquids can readily be separated from solids when a mixture of the two is dashed against a finely perforated surface. In sugar refineries centrifugalizing is the only suitable method known for separating the granulated sugar from the viscid mother liquor or molasses.

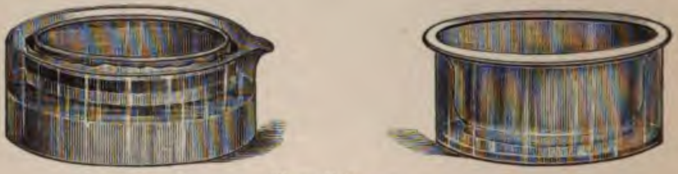
For special use in the pharmacist's laboratory, small centrifugal machines, to be operated by hand, have been devised; the outer cylinder is usually made of enamelled iron, while the inner perforated cylinder is made of porcelain; those in which motion is supplied from above are frequently provided with a cover for the inner cylinder, while in those operated from below a cover is fitted to the outer cylinder. In Figs. 149 and 150 are shown two styles of hand-power machines.

DIALYSIS.

Dialysis is a process of separation which differs entirely from those considered thus far, in not aiming at the removal of insoluble matter suspended in a liquid, but at bringing about a separation between solvents and matter held by them in solution; also between different kinds of matter held in solution by the same solvent. It is a practical application of the principle of osmosis, and is due solely to surface action and the difference in diffusibility of various substances. The word dialysis is derived from the Greek *διαλύειν*, to part asunder, to lose one from another, and was applied by Prof. Graham, of England, to the method of separation devised by him in 1861. The process consists in placing a solution of the substances to be separated on a porous diaphragm and suspending this in pure water; osmosis is established, and certain substances will pass through the diaphragm into solution in the water, while others will remain on the diaphragm, the rapidity of diffusion being in proportion to the strength of the solution and increasing with the rise in temperature. Graham discovered that crystallizable substances passed through the diaphragm freely, while amorphous bodies, such as gums, starch, gelatin, etc., either did not diffuse at all, or only very slowly; he applied the name *crystalloid* (resembling crystals) to all substances thus capable of diffusion through a septum, and the name *colloid* (resembling glue or jelly) to those substances remaining on the diaphragm. All colloids are amorphous or non-crystallizable, but all crystalloids are not necessarily capable of crystallization, as, for instance, hydrochloric acid, the most highly diffusible body, and many others. By means of dialysis, sugar can be readily separated from gum or starch, pepsin from peptones, iron salts from iron oxide, etc. Thus the process has become most valuable to manufacturers, while the analyst often finds dialysis the only means for determining the presence of certain substances in complex vegetable solutions, as, for instance, arsenous acid, corrosive mercuric chloride, or potassium iodide in compound sarsaparilla mixtures and other proprietary medicines, where the dark color and complex nature of the solution preclude all other methods of separation.

The apparatus used for dialysis is of very simple construction, as shown in Figs. 151 and 152. It consists of a circular glass vessel, with flat bottom and of convenient size, also another smaller circular but bottomless vessel of hard rubber or glass, having a projecting rim, over which is stretched a piece of bladder, parchment, or parchment paper (see page 153). The latter constitutes the dialyser proper, and into it is poured the solution to be dialysed, to the depth of about $\frac{1}{2}$ or $\frac{3}{4}$ inch, after which it is floated in distilled water contained in the other larger vessel. In Fig. 152 the glass dialyser is provided at the top with a broad rim which rests upon the edge of the outer vessel, and thus serves as a cover to protect the water against dust, etc. In place of the foregoing convenient apparatus, an ordinary clean hog or beef bladder may be used; the same should be three-fourths filled with the solution, and then suspended in a large vessel of water.

FIG. 151. FIG. 152.



Glass dialysers.

Diffusion in a dialyser will not take place unless the porous membrane or septum is in contact with water; and, moreover, its limit will be reached when the water on the outside becomes charged with such a quantity of crystalloids as to render the strength of the solution identical with that in the dialyser; hence it is necessary that the quantity of water in the outer vessel be much greater than that of the liquid in the dialyser, and that it be renewed from time to time. The crystalloids from a 10 per cent. solution of sugar, salt, or hydrochloric acid will readily diffuse through a septum if the latter is placed in contact with water, but no diffusion whatever will take place if the dialyser be floated in a 10 per cent. solution of the same substances. While the rate of diffusion varies greatly for different substances, it was found by Graham to be uniform for isomorphous bodies—that is, those having exactly the same crystalline form.

The colloidal residue remaining on the diaphragm is termed the *dialysate,* while the solution of the crystalloids that have passed through the membrane is known as the *diffusate.*

CHAPTER X.

SEPARATION OF VOLATILE MATTER.

ADVANTAGE may be taken of the volatility of some substances for the purpose of separation, and by their vaporization either of the following objects may be attained :

1. The separation of a volatile liquid from a solid, with a view to retain the solid substance, or of one liquid from another, to obtain the less volatile ; in such cases the process is termed *evaporation.*

2. When the separation of liquid and solid substances, by means of evaporation, is carried to complete dryness, the process is more particularly designated as *desiccation* or *exsiccation.*

3. The separation of a volatile liquid from either a less volatile liquid or a solid, in order to obtain and preserve the volatilized liquid for future use ; the process is then known as *distillation.*

4. The separation of a volatile solid from either a liquid or a solid which is more fixed, the object sought being the volatilized solid body ; this process is termed *sublimation.*

EVAPORATION.

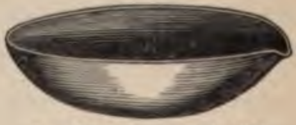
In the practice of pharmacy evaporation is extensively resorted to for the concentration of vegetable and saline solutions, the latter with a special view to subsequent crystallization, and the laws which control the process should be well understood. Evaporation may be divided into four kinds, namely, evaporation over a naked fire, on a water-bath or steam-bath, in a vacuum apparatus, and spontaneous evaporation. Evaporation over a naked fire is effected by the direct radiation of heat from a fire, on the bottom of an uncovered dish or pan, and is available when the substance in solution is not injured by direct heat or high temperature ; it is usually employed for the concentration of saline solutions for crystallization, but only when the liquid to be vaporized is water. When evaporation at temperatures below that of boiling water is desired, the low-temperature burner shown on page 81 may be used with advantage, by means of which continuous currents of hot air may be made to heat the bottom and sides of the dish, and yet actual contact of the latter with the flame be avoided.

Evaporation on a water- or steam-bath is the method most frequently resorted to ; the latter can also be employed for rapid concentration of solutions at a high temperature without the danger of injury from direct heat of the fire. Evaporation at temperatures below 100° C. (212° F.) is effected on a water-bath, and is confined to the surface of the liquid; this is the method chosen for the concentration of vegetable and other solutions liable to be injured by heat at or above that of boiling water and when more volatile solvents than water are present. Whenever a liquid is to be evaporated at a temperature below its boiling-point, rapidity of evaporation will depend upon the extent of surface exposed to the air, since the formation of vapor takes place only at the surface; hence broad, shallow vessels are to be preferred. During the boiling of liquids the rate of evaporation depends (the source of heat being constant) entirely upon the extent of surface to which heat is applied, since the more numerous the points of contact of the vessel with the source of heat the more rapid must be the formation of vapor, and ebullition is but the phenomenon of the rapid disengagement of vapor from the interior of a liquid.

Evaporation *in vacuo*, being conducted under greatly reduced pressure, is admirably adapted to the concentration of liquids holding vegetable matter in solution, but is employed only in large manufacturing establishments, owing to the complicated and expensive apparatus necessary for the operation; the process insures rapid evaporation at a low temperature, without the possibility of injury from contact with the air. In sugar refineries weak saccharine solutions are rapidly concentrated in vacuum pans to avoid coloration and inversion of the sugar. For the preparation of fluid and solid extracts, evaporation in a vacuum apparatus offers advantages not obtainable by any other method, as a low temperature and complete exclusion of air insure the retention of soluble matter in its original form as extracted from the drug. The vacuum apparatus consists of an air-tight boiler connected with a steam-bath and an air-pump operated by machinery, for exhausting the air and vapor.

Spontaneous evaporation proceeds naturally, without the use of external force, and consists in allowing vaporization to take place at the ordinary temperature. It is due to diffusion of the vapor of the liquid into the surrounding atmosphere, and its rapidity depends upon the dryness and temperature of the air; the most effectual means of promoting it, therefore, is to allow a current of warm, dry air to pass over the surface of the evaporating liquid, as this will remove the superincumbent air as soon as diffusion into it has taken place.

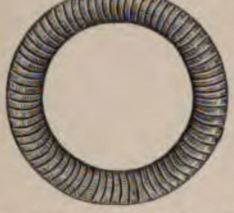
FIG. 153.



Royal Berlin porcelain dish.

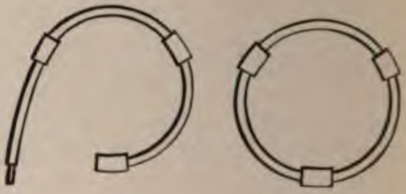
The most desirable evaporating dishes for general use are those known as Royal Berlin porcelain ware (see Fig. 153); they resist sudden changes in temperature better than other earthen vessels, and possess the great advantage of not being permeable by colored fluids. When used over direct fire, a piece of wire gauze should be interposed between the flame and the dish, so as to distribute the heat more uniformly over the bottom of the vessel and prevent the flame from striking any particular point. As glass and porcelain vessels are liable to crack when suddenly brought in contact with a cold surface after having been heated, it will prove economical to place them on straw rings or rubber grommets (see Figs. 154 and 155) when hot; these also serve admirably as supports to prevent tilting of round-bottom dishes and flasks. Grommets are easily made by forming rubber tubing into a circle and uniting the ends by means of a wooden plug; three short pieces of similar tubing of larger size are then placed one over the joint and the others at equal distances apart, which arrangement permits a circulation of air around the bottom of the vessel. Enamelled cast-iron dishes are extensively used, but, owing to the non-uniform expansion and contraction of the metal and enamel, the latter is apt to crack and chip off, unless heat be very carefully applied; the so-called "agateware" dishes are better, being made of sheet-iron and then enamelled. For neutral liquids, well-tinned copper pans may be employed; while for the evaporation of solutions of caustic soda or potassa silver or perfectly clean iron vessels are necessary.

FIG. 154.



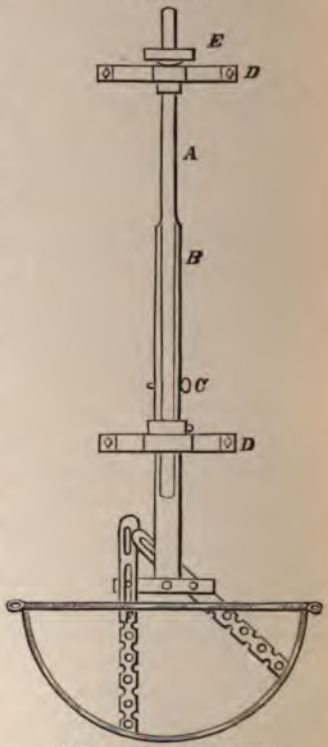
Straw ring for supporting dishes and flasks

FIG. 155.



Grommets.

FIG. 156.



Moss' mechanical stirrer.

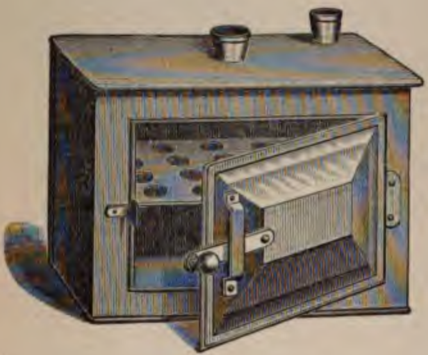
Evaporation of liquids in open vessels is materially facilitated by keeping the liquid in motion, which in small operations can be readily done by stirring with a glass rod or porcelain spatula, and on a large scale by means of a mechanical stirrer operated by steam or water power. A simple form of mechanical stirrer is shown in Fig. 156; it was devised by John Moss, of England, and consists of a $1\frac{1}{4}$ inch shaft, *A*, and a hollow shaft, *B*, which readily slides over it. These shafts are fastened together at *C*, by means of a pin, and are held vertically over the centre of the evaporating pan by means of the brackets, *D*, attached to the wall. Power for turning the shaft is supplied by a band passing around the grooved pulley at *E*. To the lower end of *B* is attached a hard-wood block, on the opposite sides of which are fastened the stirring paddles, *F*, which can be set at any desired angle, by means of winged-screw bolts, as seen in the cut. The paddles, which are usually made of ash, may consist of solid blades, 2 feet long by $2\frac{1}{2}$ inches wide and $\frac{5}{8}$ inch thick, but are preferably perforated with holes not less than 1 inch in diameter, which prevent the contents of the pan from moving around as a solid mass, and insure the formation of currents of different sizes, moving at different rates of speed, whereby evaporation is greatly facilitated.

Corrosive vapors are sometimes given off during the evaporation of acid liquids; to prevent these from contaminating the atmosphere of the store or laboratory, and also to avoid saturating the air with moisture, evaporation may be conveniently conducted under a hood communicating with a flue. When evaporation is directed to be carried to a given weight, a tared dish must be used, the dish and contents being weighed from time to time until the desired weight has been reached. If evaporation is to be carried to a given volume, the simplest plan is to measure the desired volume of water into a dish standing on a level surface, then introduce into the centre of the liquid a thin stick of wood and mark the height to which the water reaches —the liquid to be reduced in volume must be evaporated in this same dish until it stands at the point indicated by the notch on the stick.

DESICCATION.

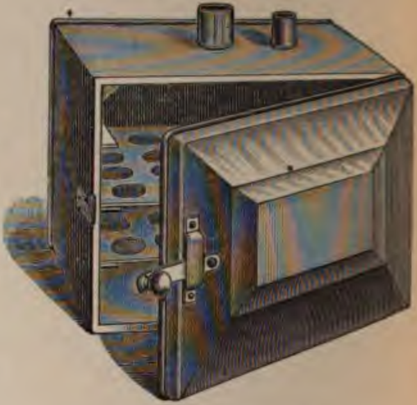
Desiccation, or exsiccation, a process of drying completely, is another method of evaporation, and is employed for driving off the moisture from vegetable drugs, crystalline salts, precipitates, pills, tablets, lozenges, etc. The temperature for effecting desiccation may vary from 40° C. (104° F.) to 200° C. (392° F.), the heating being carried on either in the open air on sand-baths or in closed compartments. For small operations, and when heat not higher than 100° C. (212° F.) is required, a portable water-oven (Fig. 157) will answer admirably. This consists of a double-walled copper box containing water, which may be heated to boiling, and thus heat supplied to the interior compartment, which is provided with a perforated tray, a closely fitting door, and an opening in the top for the escape of moisture. For temperatures above 100° C. (212° F.) a hot-air bath (Fig. 158) may be employed. This consists of a single-walled copper box through which heated air is constantly circulating, and which is provided with a thermometer through an opening in the top. In large manufacturing establishments desiccation is carried on in appropriate drying closets built of kiln-dried wood and heated by coils of steam pipe.

FIG. 157.



Hot-water drying oven.

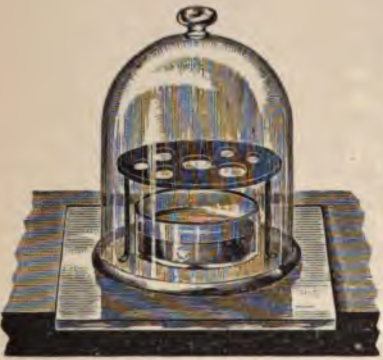
FIG. 158.



Hot-air drying oven.

The term exsiccation in pharmacy is usually reserved for a process of evaporation in which crystalline salts are first moderately heated to efflorescence, and then with constant stirring more strongly until all or most of the water of crystallization has been expelled and the powder has ceased losing weight. Dried alum, dried sulphate of iron, and dried sulphate of copper are prepared by exsiccation. Exsiccated or anhydrous salts may be restored to their original composition by simple solution in water.

FIG. 159.



Desiccator.

Desiccator is the name applied to glass apparatus of varied construction, in which substances, after having been completely dried by heat, are allowed to cool in air which is kept entirely free from moisture by strong sulphuric acid, fused calcium chloride or freshly burned lime, placed in the lower cup of the apparatus. Sometimes the desiccator is also used to abstract moisture from material which, owing to its volatile nature, cannot be exposed to heat without loss or injury, and since sulphuric acid and lime both have a great affinity for water, perfect desiccation can thus be effected. Fig. 159 represents one of the styles of this very useful apparatus, which is indispensable in quantitative chemical analysis.

INCINERATION, CALCINATION, AND TORREFACTION.

Incineration, or reduction to ash, is a process of separation applied to vegetable matter, which consists in heating it to redness in open vessels, with full access of air, until all carbon has been consumed or converted into carbon dioxide.

Calcination differs from incineration chiefly in being applied to mineral substances, which are heated to redness without fusion, for the purpose of expelling some volatile constituent at a high heat, as the carbonic acid from magnesium and calcium carbonates in the preparation of magnesia (calcined) and unslaked lime, or the nitric acid from mercuric and cupric nitrates in the preparation of the respective oxides.

Torrefaction, or roasting, is not so much a method of separation as one which is intended to modify the properties of substances by exposing them to dry heat to a point short of carbonization. Roasted coffee is probably the most familiar example. Thirty or forty years ago physicians used rhubarb, dried, and roasted in very coarse powder, which had thus lost its cathartic properties, but had retained its astringency.

DISTILLATION.

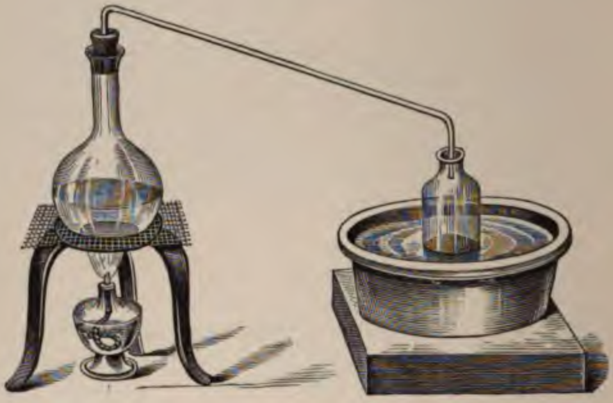
Distillation differs from evaporation chiefly in the utilization of the volatilized liquid, and in order, therefore, that no loss may occur, the process must be conducted in certain closed apparatus in which condensation of the vaporized liquid may be effected. As the application of heat to a liquid is necessary to convert it into vapor, so inversely the withdrawal of heat from vapor is essential to reconvert it into a liquid, and these two operations constitute the process of distillation; the necessary apparatus, then, must consist of two parts, a boiler, or vaporizer, and a condenser, to which may be attached a separate receiving vessel. The condensed vapor is called the distillate.

The rationale of the process of distillation may be explained as follows: Heat is applied to a liquid in a closed vessel, and is absorbed, which causes the liquid to change its state of aggregation to that of vapor; the vapor enters the condensing tube, where it comes in contact with the cold surfaces chilled by water on the outside; immediately it begins to part with its latent heat, transferring it to the cold surface and the water, and assumes again its original liquid form.

The temperature of steam not under pressure is 100° C. (212°

F.), in addition to which it carries a latent heat of 550 degrees C. (990 degrees F.); if steam is condensed and the distillate collected is to have a temperature of 50° C. (122° F.), at least 600 degrees C. (1080 degrees F.) of heat must be given off or transferred to the water in the cooler. In other words, each liter of water converted into steam requires 6 liters of water at 0° C. (32° F.) to convert it back into water having a temperature of 50° C. (122° F.).

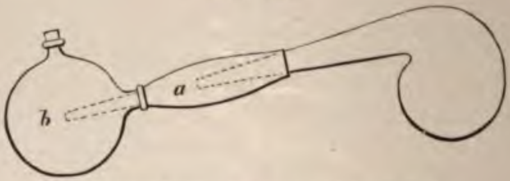
FIG. 160.



Simple distillation from a flask.

Alcoholic vapor requires only about one-half as much cold water for condensation as aqueous vapor, since its sensible heat is 78.2° C. (172.7° F.) and its latent heat only 215 degrees C. (387 degrees F.). The sensible heat of the vapor of official diluted alcohol is 82° C. (179.6° F.), and its latent heat about 260 degrees C. (468 degrees F.).

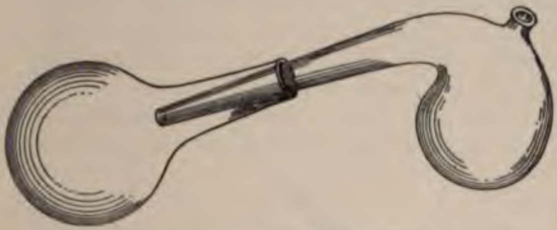
FIG. 161.



Plain retort with adapter, *a*, and receiver, *b*.

As such large quantities of water for condensing purposes are not practically available, the same object is attained—the withdrawal of the latent heat from vaporized liquids as completely as possible—by a continuous supply of cold running water. It has been frequently observed in the preparation of distilled water that more rapid condensation takes place if the water surrounding the condenser be supplied slowly and thus allowed to become warm. The outlet, or lower end of the condensing tube, should always be kept coolest, hence cold water must be supplied at this point and carried upward. Care must also be observed that the application of heat and refrigeration be properly adjusted, so that vapor be not generated in excess of the capacity of the condenser.

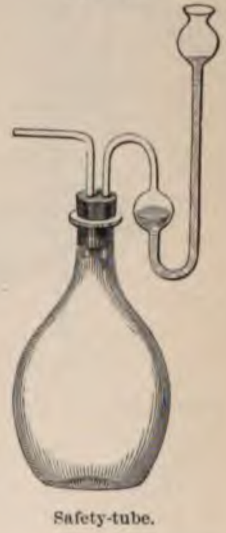
FIG. 162.



Tubulated retort and flask receiver.

The simplest form of distillatory apparatus consists of a flask, or retort, in which the liquid to be distilled is vaporized, and a receiver immersed in cold water, in which the vapor is condensed. When a flask is used, this is connected with the receiver by means of glass tubing, as shown in Fig. 160, while in the case of the retort connection is made either by means of an adapter, see Fig. 161, or by inserting the beak of the retort directly into the receiver, as shown in Fig. 162.

FIG. 163.



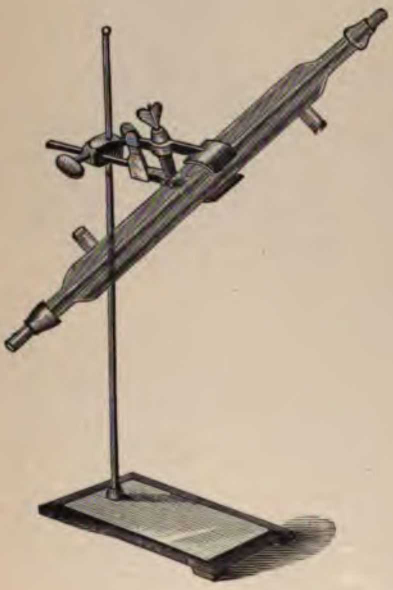
Safety-tube.

To cool the vapor still more thoroughly, the beak of the retort, or the tube connecting the flask with the receiver may be wrapped in part with cotton cloth upon which a constant stream of cold water is allowed to trickle, the water being prevented from running into the receiver by suspending the end of the cloth in the receptacle for waste water. Tubulated retorts have almost entirely superseded the plain variety, as they possess the advantage of being more easily filled and cleaned, and also admit of the introduction of a thermometer or safety-tube, through a cork in the tubulure. A safety-tube, Fig. 163, is often necessary in distillation from retorts or flasks, to allow the escape of large volumes of vapor accumulated and suddenly evolved, which otherwise might endanger the apparatus or cause the liquid to rise and flow over into the condensing tube. Wide-mouth, flat-bottom flasks are preferable to retorts, as they can be

more readily filled, connected and cleaned, and are easily suppor
on a sand- or water-bath.

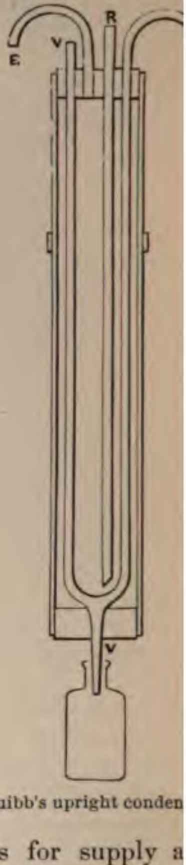
For many purposes, when the most perfect refrigeration of va
possible is desired, the apparatus known as the Liebig conden
will be found extremely useful, its construction being such as to
sure a constant supply of cold water around the condensing tu
which can be readily connected with any flask or retort by me
of corks and glass tubing. The Liebig condenser consists of t
tubes, one within the other; the inner always of glass, the outer

FIG. 164.



All-glass Liebig condenser, with adjustable clamp.

FIG. 165.



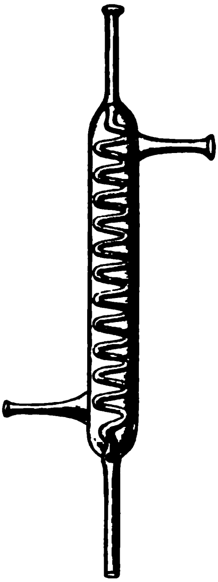
Squibb's upright conden

glass or metal and provided with attachments for supply a
waste of water, which is made to enter near the lower end a
to traverse the whole length of the outer tube before it is c
charged at the upper end; therefore, as the vapor passes dow
ward in the inner tube it is continually cooled, and thus perf
condensation effected before it reaches the receiving vessel. F
164 shows an all-glass Liebig condenser attachable to any filteri

stand and capable of being set at any angle or height, by means of the clamp support, to suit the position of the flask or retort with which it is to be connected.

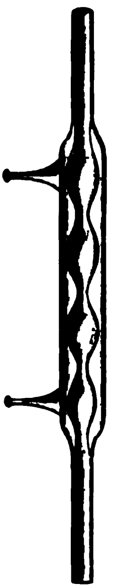
In order to economize space on the laboratory table, the late Dr. Squibb devised an upright condenser, also made of glass, which can be attached, like the preceding one, to a stand; it is very effective, and differs from the Liebig condenser in having the condensing tube doubled like a U, shown in Fig. 165. The outer lines represent the water-case tube, V V the vapor tube of U-shape with a small opening at the lower end, from which the condensed liquid escapes to a proper recipient, while any uncondensed vapor passes to the other leg of the tube, is there condensed, and flows downward to the outlet. R is the tube supplying cold water to the lower end of the water case, which rises and finally flows out through E.

FIG. 166.



Reflux condenser.

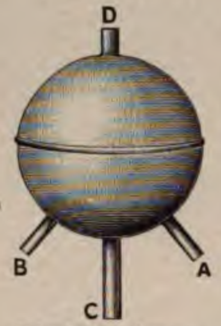
FIG. 167.



Reflux condenser.

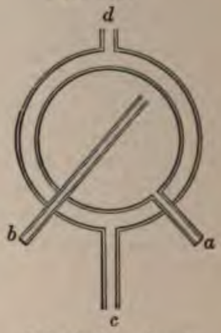
Condensers intended for special purposes are often made of different designs, the same principle, however, being applied in all, namely, to bring the vapor in contact with a cold surface, kept so by a continuous supply of cold water. Thus the glass upright or reflux condensers shown in Figs. 166 and 167 are intended to be used in connection with a flask or an extraction apparatus for the purpose of condensing the vapor of alcohol, chloroform, ether, and similar liquids, and allowing the condensed fluid to flow back into the vessel from which the vapor issued. The spherical condenser, Fig. 168, is usually made of brass, and occupying less space is preferred by many to the upright condensers; it is intended for the same purposes as the latter. A sectional view, shown in Fig. 169, explains the construction; the cold water enters at *a*, and filling the inner space is allowed to flow out at *b*, while the vapor passes into the annular space surrounding the water reservoir, through the tube *c*, and having been condensed flows back again through *c*; the tube *d* is usually kept loosely corked, and is simply a safety attachment

Fig. 168.



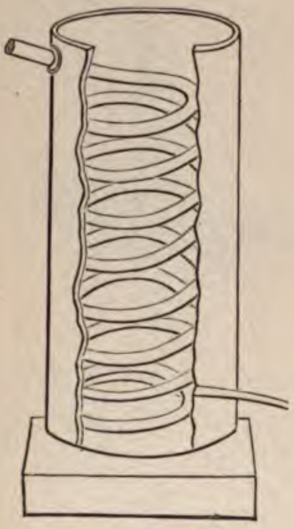
Spherical condenser.

Fig. 169.



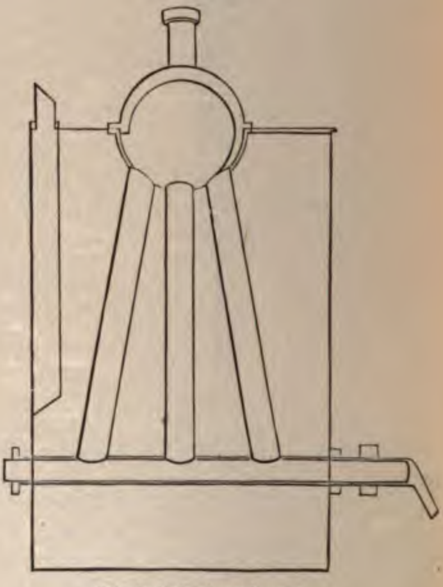
Spherical condenser.

Fig. 170.



Worm condenser.

Fig. 171.

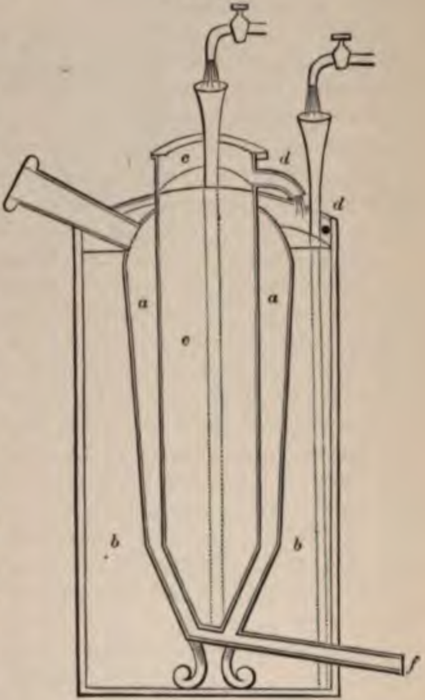


The Beindorf condenser.

to allow the vapor to escape in case it should fail to be completely condensed.

For large operations, condensation of vapor is usually effected in a metal or stoneware tube bent in the form of a spiral, and known as a *condensing worm* (see Fig. 170), inclosed in a metal or wooden case, which is kept supplied with a constant stream of cold water. On account of the difficulty encountered in cleaning the worm, other arrangements have been suggested, some of which are extensively employed in Europe. Fig. 171 represents the *Beindorf condenser*, in which the vapor is made to pass through three straight tubes, connecting with a common outlet tube; by unscrewing the upper half of the globular chamber into which the vapor first passes, all the tubes can be thoroughly cleansed. The *Mitscherlich condenser* (Fig. 172) differs from others in keeping the vapor in contact with two separately cooled surfaces, which insures more rapid condensation; as shown in the illustration, the condensing chamber consists of a somewhat tapering cylindrical vessel, *a*, ending in a tube, the whole made of metal (preferably block-tin), and resting on a support in a large metal or wooden case, *b*; into this condenser is accurately fitted at the shoulder a similar metal cylinder, *c*, cone-shaped at the closed end. By means of long funnel tubes cold water is continually supplied at the bottom of the outer and inner coolers, *b* and *c*, which rises as it becomes warmed, and flows out at the top at *d* and *d*; the distillate flows off into a receiver at *f*. In practice the Mitscherlich condenser has been found very effective, and if the inner cooler has been properly fitted to the condensing chamber, no escape of vapor need be feared; it is readily taken apart and cleaned, and the only apparent disadvantage lies in the double water supply and waste.

FIG. 172.

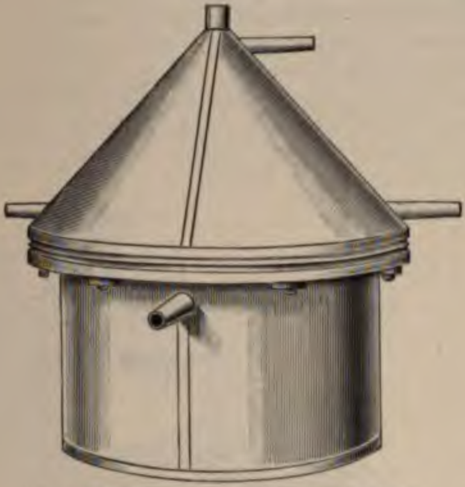


The Mitscherlich condenser.

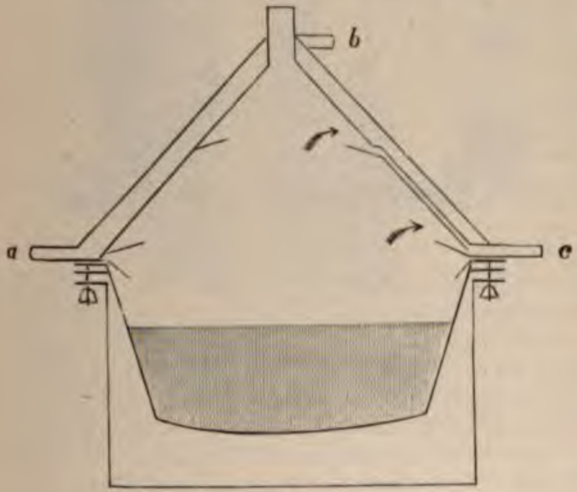
It frequently happens, when distilling from glass flasks or retorts, that the liquid, although boiling at first quietly, suddenly begins to evolve vapor violently, the phenomenon repeating itself from time to time. This outburst of accumulated vapor is termed *bumping*, and although it has not been satisfactorily explained, it is known to occur chiefly in smooth glass vessels; it is both annoying and dangerous, as it may result in fracture of the vessel, or in the liquid splashing upward into the condensing tube. Bumping may be due to unequal heating of the vessel, for if the flask or retort be covered with a hood of paste-board or metal, so that the heat be equally diffused, it occurs but rarely and less violently. Another remedy consists in introducing angular bodies into the liquid, such as pieces of pumice-stone or glass, or a long platinum spiral, which will afford a ready means of escape for the vapor from the bottom of the liquid. Prof. Proctor, of England, has proposed as a very effectual remedy, to pass a slow current of air, hydrogen, or carbon dioxide through the hot liquid; for small operations this may be done by forcing a stream of air, by means of an India-rubber ball bellows, through a glass tube drawn out to a capillary tube and dipping to the bottom of the liquid, while heat is being applied. Ebullition is said to go on smoothly so long as this is continued, but bumping commences as soon as the .supply of air ceases. Another plan which has been found very satisfactory, especially in the process of distillation, is the suction of air through the retort by means of an aspirator attached to the receiver.

For the recovery of alcohol from weak percolates in the concentration of vegetable solutions by distillation, special metallic stills have been devised. Those made of heavily tinned copper, of 1- to 5-gallon capacity, will be found most desirable for pharmacists. Figs. 173, 174, 175, and 177 represent different styles of pharmaceutical stills in use at the present time. Beck's pharmaceutical still (Fig. 173) is one of the best stills made for the concentration of weak percolates and the recovery of alcohol, and is especially adapted for the work of the small manufacturer. It is simple in construction, efficient in condensing power, and easily cleaned. It is made of heavily tinned copper, and the evaporating pan has a capacity of 2 gallons. The cold water, which is made to circulate freely between the double walls of the cone-shaped head, is supplied near the base on one side, at *a*, and discharged at the top on the other side, at *b*. The vapor is condensed on the under side of the still-head, the distillate collecting in two gutters or troughs, one above the other, whence it is discharged through a common outlet, *c*, as shown in the sectional view. The water-bath and condenser are securely clamped together by means of six bolts and nuts, the rim of the evaporating pan being interposed between two flat rubber rings; an air-tight joint is thus produced and escape of vapor effectually guarded against. A small tube on the side of the water-bath is for the escape of steam, and if about 1½ gallons of water be put into the bath when the still is started, it will not require refilling for about twenty-four hours. If the quantity of liquid to be distilled is in excess of the capacity of the evaporating dish, the latter may be refilled by means of a long-stem funnel through the opening in the apex of the still-head. The important features of the Beck still are: 1. A broad and rather shallow evaporating dish; since the liquid will be kept at a temperature below its boiling-point, vaporization will take place wholly at the surface, and hence the larger the surface exposed the more rapidly will the vapor escape. 2. The two gutters or troughs on the under side of the still-head, whereby the dripping back of any con-

Fig. 173.



Beck's pharmaceutical still (exterior view).

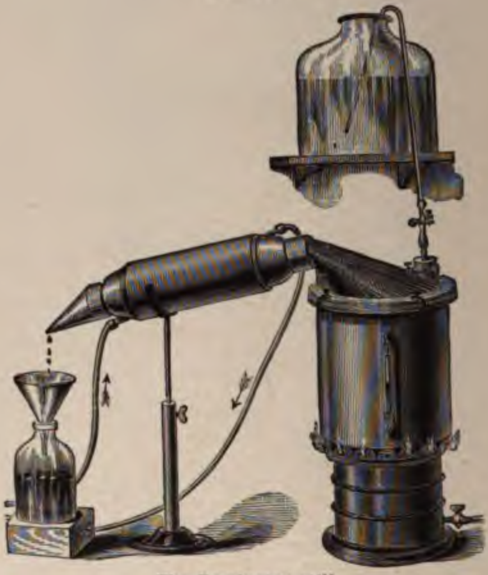


(Sectional view.)

densed liquid into the evaporating dish is avoided, and thus the annoying feature of a single-gutter arrangement overcome. 3. The capacity and style of the water-bath, which are such as to insure a supply of hot water or steam under and around the evaporating dish for many hours, since the escape of steam at the temperature employed is quite moderate. The Beck still can be heated with either gas or oil, and if water attachments are not convenient, a barrel of cold water may be placed at some height above the still, from which the condenser can be supplied.

The special features of the Remington still (Fig. 174) are the peculiar shape of the still-head and the construction of the condenser.

Fig. 174.



The Remington still.

In the former the opening for the passage of the vapor is drawn over to one side, instead of being in the centre as usual, by which arrangement the condensing surface of the head is greatly reduced and condensation of vapor within the body of the still obviated as far as possible. The condensing tube represents a multiple Liebig condenser, 7 block-tin tubes being so arranged within a copper case that cold water is constantly circulating between them. Two ground-brass joints are used—one at the point of juncture of the condenser with the still-head, the other where the nose-piece is attached to the end of the condenser. The capacity of the still is 3 gallons, and by the siphon arrangement shown in Fig. 174 it is possible to feed the still from a reservoir while distillation is in progress.

The Prentiss alcohol-reclaimer (Fig. 175) is easily operated. It is made of tinned copper, and is provided with an upright column, B, screwed to the top of the still, in which is placed a rod carrying a series of perforated tin disks (see Fig. 176) intended to increase the alcoholic strength of the distillate by condensing the aqueous vapor, which then returns to the still, while the vapor of alcohol passes on to the condenser proper. The vapor passes from the column through a short tube, C, to the condenser, which consists of a 12-ounce copper can, D, containing a tube bent zigzag, and supplied with cold water by means of a funnel tube, E, reaching to the bottom of the can. The distillate is collected at the outlet, G, a continuation of the zigzag condensing tube, while the waste-water flows out at F, which is connected with the sink by means of rubber tubing.

FIG. 175.

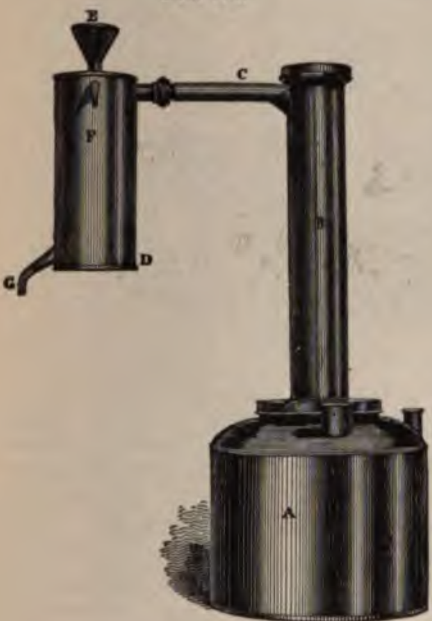
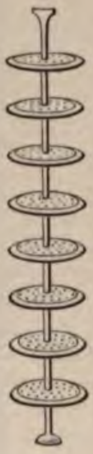


FIG. 176.

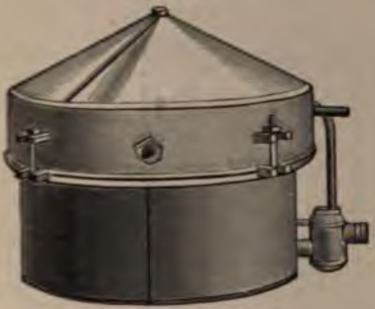


The Prentiss alcohol-reclaimer.

The Anderson automatic still (Fig. 177) differs from the others described in the continuous automatic supply of water to the water-bath. The refrigeration of vapor is effected by a free circulation of water between the walls of the cone-shaped condenser, as in the Beck still, the distillate collecting in a gutter at the base of the cone. The water in the condenser gradually becomes warm and flows into the water-bath, which is kept filled to a uniform height by means of an overflow pipe, and thus the necessity of replenishing the boiler with cold water from time to time, in large operations, is obviated. The liquid to be distilled is heated in a broad, shallow evaporating dish, from which the alcoholic vapors rise rapidly owing to the large extent of surface exposed.

Automatic stills are recommended and largely used for the distillation of water; but when absolute purity is desired it must not be overlooked that in automatic stills the air and other gases contained in the water are sure to pass out with the steam and redissolve in the condensed vapor, so that, while all non-volatile impurities are removed, volatile matter is sure to contaminate the distillate. Distilled water entirely free from air and all other impurities can be obtained only by rejecting the first portion of the distillate (about 10 per cent.), which contains the volatile matter, and allowing the last portion (about 10 per cent.) to remain in the still; this will retain all mineral impurities and such decomposition products as may result from the prolonged action of heat on organic constituents. Only about 80 per cent. of the volume of water to be distilled should be collected and considered absolutely pure. The tubes in which the aqueous vapor is condensed must be of glass or pure block-tin.

FIG. 177.

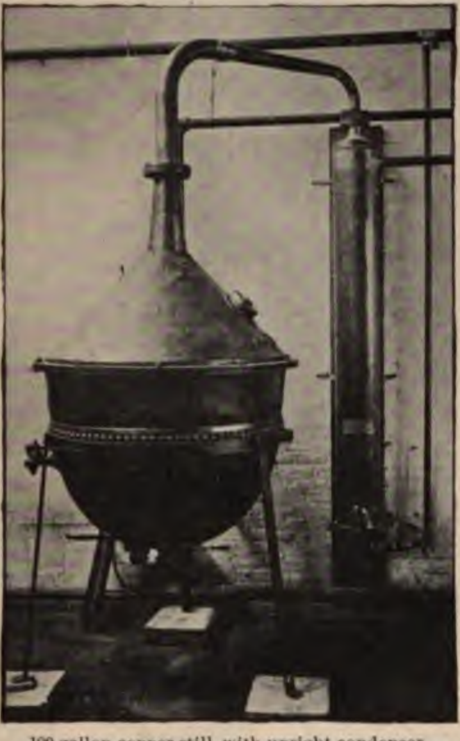


The Anderson automatic still.

In the manufacture of fluid and solid extracts and similar preparations, on a large scale, stills heated by steam are employed for the concentration of weak percolates and the recovery of alcohol. Such stills are made of heavily tinned copper, and will hold from 50 to 250 gallons of percolate. The boiler, or evaporating pan, is partly enclosed in a copper jacket provided with an inlet and outlet for steam, by which means heat is supplied to the liquid. Fig. 178 represents one of these large steam stills. Condensation of the alcoholic vapor is effected by either a worm or an upright condenser, the latter usually consisting of a number of straight block-tin pipes encased in a copper cylinder, on the principle of the Liebig condenser.

The still designed by Dr. Rice (see Fig. 179) presents the peculiarity of having the condenser situated immediately above the still-head, which is for the double purpose of saving floor-space and allowing the condenser to be used as a reflux condenser in the case of continuous percolation, as explained below. The case enclosing the condensing coil is made of copper, has a rounded bottom, and is closed at the top; cold water is supplied at the bottom at B by means of the rubber tube A, and is discharged at C, near the top, by means of a tube leading to the waste-pipe D. The small tube near B, usually closed with a cork, is for the purpose of emptying the water without removing the tube A. The head of the still is provided with three short tubular openings, one for refilling the still when required, another for inserting a thermometer, and the third, shown in the cut, for carrying a safety tube, L. The vapor-pipe starts from the still-head at E, and is connected with the projecting end of the block-tin condensing coil, near the upper part of the tank, at E. The worm inside of the condenser tank has a uniform downward descent, and emerges at F, extending a short distance to the joint, by means of which it is connected with a block-tin pipe, J, leading to the receiving vessel. The head is attached to the body of the still by means of a rubber washer and iron clamps, and can be readily

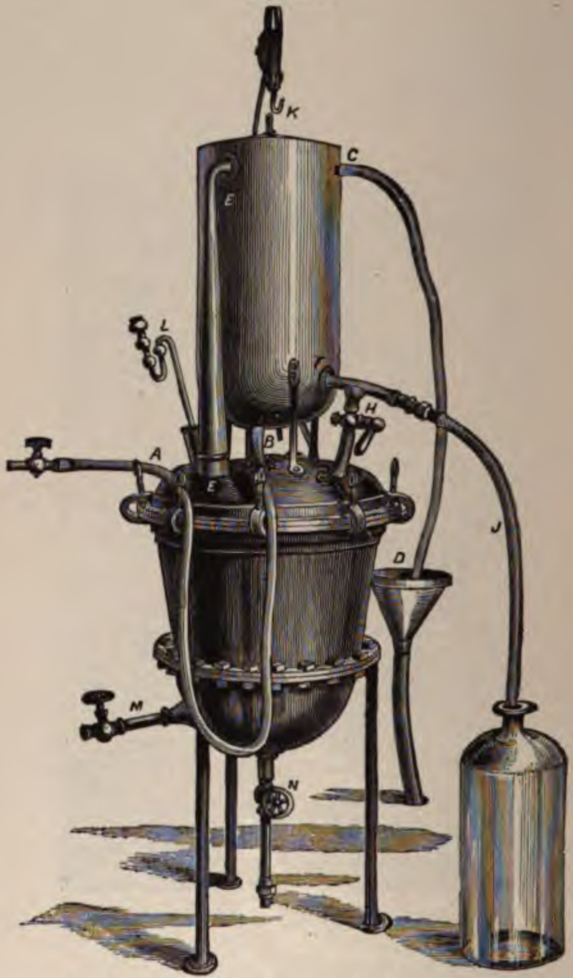
FIG. 178.



100-gallon copper still, with upright condenser.

removed, after taking off the clamps, by attaching the tackle K to the top of the condenser and hoisting the whole upward. Steam is admitted to the jacket at M, and N is the exhaust pipe for the same.

FIG. 179.



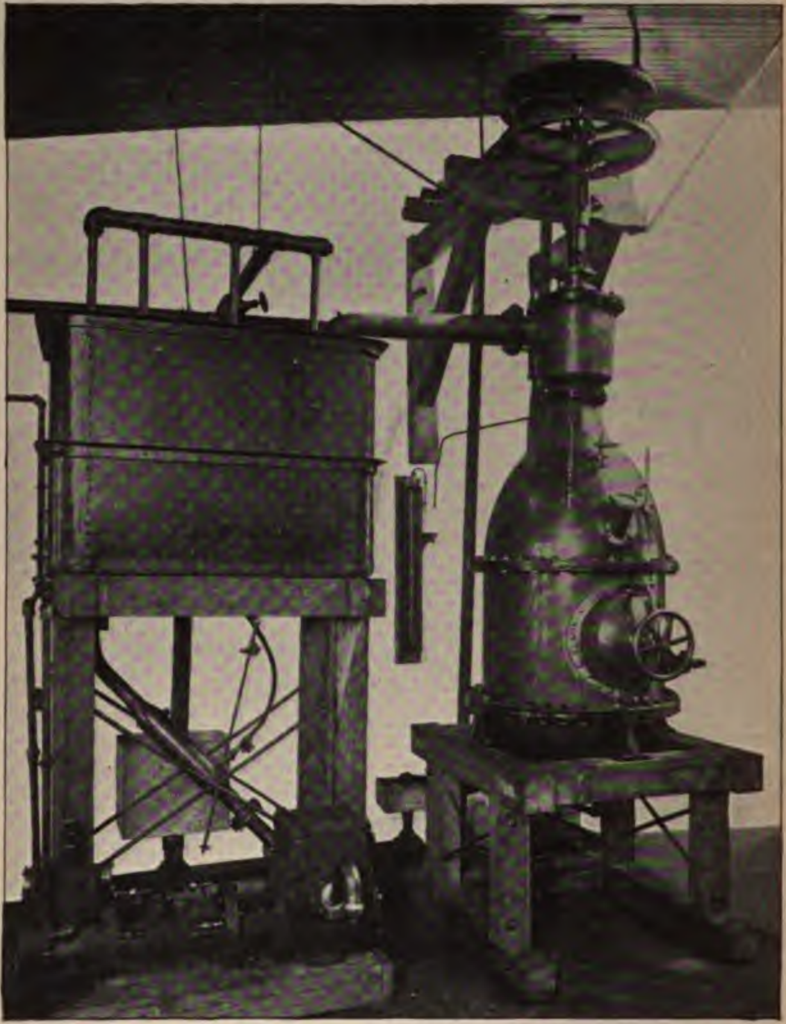
Still and condenser designed by Dr. Charles Rice.

About the middle of the lower projecting end of the condensing tube a branch passes downward back to the still at G, and terminates under the head in the form of an ∽ , which trap prevents any condensed liquid from flowing back into the still should the stopcock at H be open. The object of this branch pipe is to carry the condensed alcohol back to the still when the apparatus is used for continuous percolation of such substances as nux vomica, aconite, etc. When the still is to be used for this purpose, a large tin-lined copper percolator, into which the moistened drug has been packed and covered with a felt diaphragm, is securely clamped between the head and the body of the still, into which menstruum has previously een poured. When steam is admitted to the jacket the alcohol is aporized, recondensed in the condenser above, and made to flow ck to the still and on to the drug in the percolator by means of e branch pipe and stopcock at H, the tube J having been discon-cted and the joint closed with a cork. The percolate collects in e body of the still and the alcohol is again vaporized as before, the ocess continuing at the pleasure of the operator, and the drug ing thoroughly exhausted with a minimum quantity of menstruum. us, prolonged digestion and continuous percolation of large quan-ies of drugs can be successfully carried on in this apparatus with-t any loss of alcohol.

The so-called dreg stills for the recovery of alcohol from the arc are sometimes made of 300 or 500 gallons capacity, of heavy pper, but not jacketed; as no injury can be done to the exhausted aterial by heat, live steam is passed directly into the still-body ntaining the marc, and the alcohol is thus rapidly vaporized and rced into suitable condensers.

Vacuum stills are necessarily of a somewhat different construc-on, and are used only in large manufacturing establishments, here the concentration of bulky vegetable solutions at low tem-eratures is frequently desired. Without the use of vacuum appa-tus the evaporation of solid extracts, without injury, to a con-tion suitable for powdering, would be an impossibility. Fig. 180 presents a large vacuum still in operation at the establishment Sharp & Dohme, of Baltimore, who have kindly granted the ivilege of giving a photographic reproduction of the apparatus. e still proper consists of an egg-shaped vessel of heavily tinned pper, partly encased in a jacket, to which steam is supplied; it provided with a vacuum gauge, thermometer, sight-glasses through hich the process of evaporation may be watched, and an in-enious stirring apparatus attached to the vertical shaft, operated y means of the two geared wheels seen above the still. The quid to be evaporated is supplied automatically through the tube een projecting from the side of the still, to the right of the wheel which operates the clamp holding the man-hole cover in posi-ion. Cleaning of the still is effected through a large man-hole in he lower front of the still-body. The vapor of the evaporating iquid passes through the large tube projecting laterally from the till-head, into a series of condensing tubes resting in a large iron ank provided with a constant supply of water; any vapor escaping ondensation in these tubes, which may happen on account of its ore rapid movement caused by the action of the vacuum pump, ill be caught and condensed in the Liebig condenser situated diagonally underneath the iron tank. The distillate is finally discharged through the large spout which may be seen emerging from the valve box connected with the pump about the centre of the lower part of the figure.

FIG. 180.



Large vacuum still and condensing tank.

The rarefaction of air in the apparatus is accomplished by means of an exhaust pump situated under the condensing tank and communicating with the condensing tubes.

When the still is to be operated, the pump is started, exhausting the air from the still until the desired vacuum is reached, as indicated by the barometric gauge attached to the wall between the still and the condensing tank, and connected with the still by means of a two-neck bottle and a block-tin pipe. A rubber hose dipping into the liquid to be evaporated is then connected with the projecting tube to the right of the man-hole, and the stopcock in the tube having been opened, the liquid is allowed to flow into the still by atmospheric pressure until it reaches the desired height in the still, after which the stopcock is partially closed and so set that the supply of liquid is automatically kept up in proportion to its evaporation—the aim being to preserve, as far as possible, the original volume of the liquid in the still. By this arrangement large volumes of percolate can be concentrated in a comparatively short time, without taking the still apart or interfering in any way with the distillation of the menstruum. Evaporation taking place at a low temperature and with entire exclusion of air, no possible injury can occur to the constituents in solution.

Fractional distillation is the name applied to a process intended to separate liquids of different boiling-points, and is often a valuable aid in determining the composition of a mixture or in the purification of certain chemicals. It necessitates the introduction of an accurate thermometer into the retort, flask, or still, so that a change in the boiling-point may be promptly observed and the receiving flask changed accordingly. As all liquids will begin to vaporize before their boiling-point is reached, perfect separation is impossible in a single operation; it is, therefore, customary to collect the liquids condensed during a certain range of temperature in the still, and to subject these again to the same process of fractionation, until finally a pure liquid showing a stationary boiling-point is obtained. As an example, may be cited a mixture of ether, chloroform, and alcohol. If pure, the three liquids will boil at 35.5° C., 60.5° C., and 78° C., respectively; but a mixture may possibly boil at about 40° C., when almost all of the ether will distil over, together with small portions of chloroform and traces of alcohol. As the temperature rises to 65° C. the distillate will consist chiefly of chloroform mixed with traces of ether and small portions of alcohol; and finally, at 78° C., alcohol will distil over, not, however, entirely free from chloroform and traces of ether. By changing the receiving flask at 40° C. and 65° C., fractions will be obtained entirely different in composition from the original. If the first fraction be now distilled, the liquid will probably boil near 38° C., and by carefully watching the thermometer and changing the receiver ether almost entirely free from chloroform and alcohol may be obtained. By thus carefully collecting the fractions at fixed temperatures, and re-distilling each by itself, more thorough separation is possible.

During the ebullition of a pure liquid no change of temperature will be indicated by the thermometer, but in a mixture of intersoluble liquids a gradual rise will continue as the more volatile are vaporized, this rise being slow or rapid as either the more volatile or less volatile liquids predominate. If a mixture of only partly miscible liquids be subjected to distillation, the temperature will remain stationary during the ebullition of the more volatile liquid and only begin to rise when the same has nearly all been vaporized. In such cases almost perfect separation can be effected, particularly if the boiling-points of the liquids lie far apart. Examples: benzin and alcohol, or alcohol and oil of turpentine. Numerous coal-tar products are obtained by fractional distillation.

Fractional condensation is closely allied to fractional distillation, and is largely employed in the rectification of alcohol and the purification and concentration of glycerin and other liquids. It is effected by passing the mixed vapors into a series of condensers kept at regular temperatures, each succeeding one being cooler than the one which precedes it.

Destructive distillation is the process of heating dry vegetable or animal matter, in suitable closed vessels, until decomposition takes place, the volatile products being expelled and a fixed residue remaining. As the name indicates, the process involves the destruction of the original compound, whereby products of simpler composition are obtained. In order to avoid oxidation, destructive distillation must be carried on in closed apparatus with entire exclusion of air, and as the heat necessary is in most cases far greater than that to which glass vessels could be safely exposed, iron retorts or cylinders are employed. The residue left in the iron retort is often a fused mass insoluble in water, which necessitates mechanical means for its removal. The products of destructive distillation, in their crude state, are usually accompanied by a peculiar smoky odor called *empyreuma*, said to be due to an oil developed during the process of decomposition; this is subsequently removed by rectification. The most striking examples of destructive distillation are the manufacture of acetic acid from wood and of illuminating-gas from coal.

SUBLIMATION.

Sublimation is the term applied to the process of vaporizing volatile solids and condensing the vapor back into a solid; it must not be confounded with the term *dry distillation*, which is frequently used in place of destructive distillation. The product of sublimation is known as a sublimate, and may occur in the form either of a fine powder or compact masses.

The object of the process of sublimation may be the purification of a substance by separating the volatile solid from less volatile or fixed impurities, as in the case of sulphur, camphor, naphtalene, and iodine, or the separation and collection of volatile solids resulting from chemical reaction at higher temperatures, as in the case of pyrogallol, calomel, and mercuric chloride.

The apparatus consists of a subliming vessel made of iron, glass, or earthenware, and a condenser adapted to the volatility of the product, the condensing surface being kept sufficiently near the source of heat to avoid cooling of the vapor before it reaches the condenser. If the temperature of the condenser is but little below that of the subliming vessel, the vapors of the volatilized substance will not condense until they strike the surface of the condenser, and will form in compact masses, frequently in crystalline condition; as, for instance, arsenous acid, corrosive mercuric chloride, ammonium carbonate, and commercial sal-ammoniac. In order to obtain the sublimate in the form of powder, the air in the condenser must be decidedly cooler than the temperature at which the substance volatilizes, because then the vapor will be immediately cooled and rapidly deposited in very small particles, as in the case of calomel, sulphur, and camphor when intended for subsequent compression.

The process of sublimation is confined to the larger operations of manufacturing chemists, but can be demonstrated in a small way by placing a few grains of camphor or iodine in a long test-tube and then heating until all has been volatilized; in a few minutes the substance may be gathered in the form of very small crystals from the upper part of the tube.

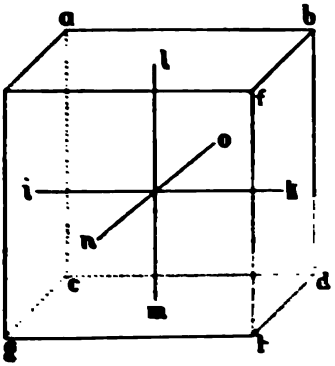
CHAPTER XI.

CRYSTALLIZATION.

THE subject of crystallization, while a most important l mineralogy and chemical physics, is of less value in proper; but as the Pharmacopœia makes frequent use belonging to the study of crystallography, and as the p may have occasion to resort to crystallization for the p determining the character and quality of substances, a sh is deemed desirable.

Crystallization may be looked upon as another method tion, as it is frequently employed for the purpose of impurities from crystalliz stances. The term *cryst* plied to solid inanimate l regular internal structure nite geometrical form, bo plane surfaces and havir of fixed and constant valu assumption of such distinc metrical forms occurs, a during the change taking the state of aggregation stances from the gaseous to the solid condition; i cases it occurs also in soli as iron and brass wire.

FIG. 181.



In the preliminary s crystallography the meaning of the following terms mus sidered.

Faces are the plane surfaces bounding the crystal (see *a* *abfe*, and *efhg*, Fig. 181).

Edges are the lines of intersection of two adjoining fac *ab*, *fh*, [illegible] etc., Fig. 181).

Angles are the points formed by intersection of thre faces (see Fig. 181, *e*, formed by [illegible] and *efhg*; by [illegible] formed by [illegible] and *aegc*

Axes are imaginary lines drawn through the center of tal, around which the symmetrical deposit of matter has during the formation of the crystal (see *ik*, *lm*, and *no*, Fig

Amorphous (without form) designates the absence of c form and structure, as in acacia, starch, gelatin, etc.

Dimorphous or *trimorphous* (of *two* or *three* forms) indicates that the substance occurs in two or three distinct crystalline forms, as carbon, sulphur, etc.

Polymorphous means of many forms.

Isomorphous (of the same form) indicates that two or more substances to which the term is applied crystallize in the same form; thus the chlorides, iodides, and bromides of sodium and potassium are isomorphous. Isomorphous bodies are known to resemble each other also in chemical composition, and to permit of a ready interchange of constituents, as in the case of the various alums.

Cleavage is the tendency of most crystals to split in particular directions, affording usually even and frequently polished surfaces, the direction being always parallel with the planes of the axes, or with others diagonal to these. While some crystals cleave very easily, in others this tendency is scarcely discernible.

Tabular crystals are such as crystallize in flat plates, as potassium chlorate, iodine, strontium iodide, etc.

Laminar crystals are such as crystallize in thin plates, as acetanilid, naphtol, calcium hypophosphite, etc.

Acicular crystals are such as occur needle-shaped, as aloin, cinchonidine sulphate, quinine salts, etc.

Prismatic crystals are such as resemble a prism, being extended chiefly in the direction of the longest axis, as salicylic acid, santonin, cinchonine sulphate, etc.

Orthometric refers to the measurement of the angles, and is used to signify that the three axes intersect each other at right angles.

Clinometric refers to the intersection of the axes at oblique angles.

Holohedral, applied to crystalline forms, signifies that the full number of faces required by perfect symmetry are present.

Hemihedral signifies that only one-half the number of faces required by full symmetry are present.

Crystals are formed according to fixed laws of Nature, and there can be no doubt that the force of cohesion plays an important part in their formation; but no one knows how, nor why, the molecular particles of certain substances arrange themselves into symmetrical deposits, around a common centre, in a manner to give rise to numerous distinct and definite forms.

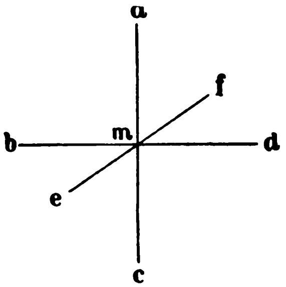
The large variety of forms in which crystals appear depends entirely upon the number and length of the axes and their relative inclination—that is, the angles at which they intersect each other. All crystalline forms have been reduced by scientists to two main groups, the *orthometric* and the *clinometric* groups (see above), and these have again been subdivided into six systems: the orthometric group comprises the *regular*, *quadratic*, *rhombic*, and *hexagonal* systems; the clinometric group, the *monoclinic* and *triclinic* systems. As all crystals belong to one or the other of these systems, the salient features of each should be studied.

1. *The Regular System*, also known as the Monometric, Cubic, Octahedral, or Tessular System.

Crystals of this system have three axes of equal length, which intersect each other at right angles, as shown in Fig. 182.

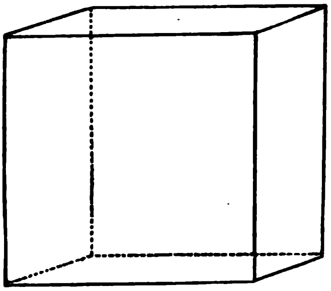
The fundamental forms of this system are the cube and the octahedron (Figs. 183 and 184).

FIG. 182.



Axes of the *regular* system.

FIG. 183.

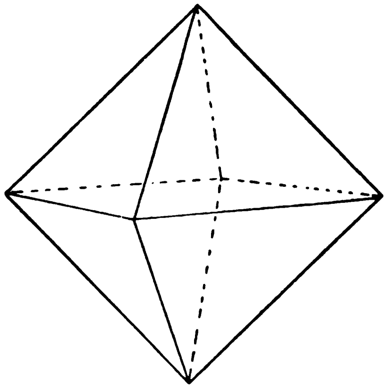


The cube.

Alum, phosphorus, arsenic trioxide, diamonds, alkali iodides, chlorides, fluorides, and cyanides, as well as many metals and their sulphides, crystallize in this system.

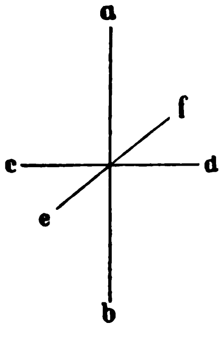
2. *The Quadratic System*, also known as the Dimetric, Square Prismatic, or Tetragonal System.

FIG. 184.



Regular octahedron.

FIG. 185.

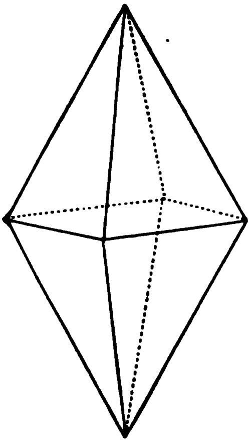


Axes of the *quadratic* system.

Crystals of this system have three axes intersecting each other at right angles, two of which are of equal length and one either longer or shorter than the other two; the two equal axes are called secondary axes, while the third is termed the primary axis (see Fig. 185).

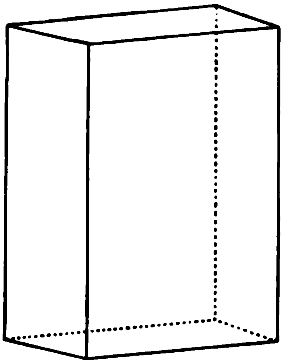
The fundamental forms of this system are the quadratic octahedron (also called square-based double pyramid) and the right-square prism (Figs. 186 and 187). The pyramids of this system have square bases.

FIG. 186.



Quadratic octahedron.

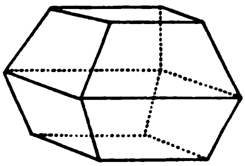
FIG. 187.



Right-square or quadratic prism.

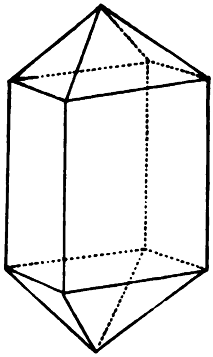
Among the modified forms are the truncated quadratic octahedron Fig. 188) and the quadratic pyramidal prism (Fig. 189).

FIG. 188.



Truncated quadratic octahedron.

FIG. 189.



Quadratic prism with pyramidal ends.

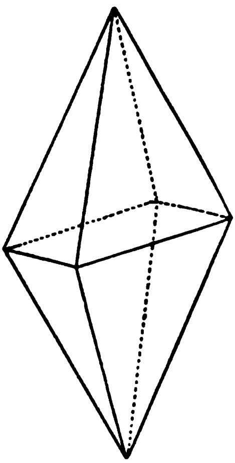
Potassium ferrocyanide, calomel, nickel sulphate, boron, tin, tannic oxide, magnesium sulphate, zinc sulphate, etc., crystallize in this system.

3. *The Rhombic System,* also known as the Trimetric or Right Prismatic System.

Crystals of this system have three unequal axes intersecting each other at right angles, shown in Fig. 190. The fundamental form of this system is the rhombic octahedron or right rhombic double pyramid (see Fig. 191). A modified form is the rhombic six-sided prismatic pyramid (Fig. 192).

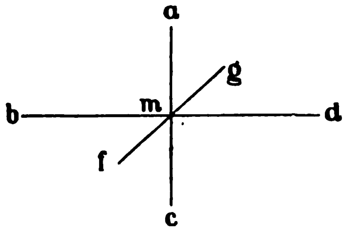
Potassium sulphate and nitrate, resorcin, zinc sulphate, citric acid, iodine, Rochelle salt, mercuric chloride, barium chloride, tartar emetic, codeine, salicylic acid, piperin, Epsom salt, silv— nitrate, ammonium sulphate, cream of tartar, etc., crystallize in th— state.

FIG. 191.



Rhombic octahedron.

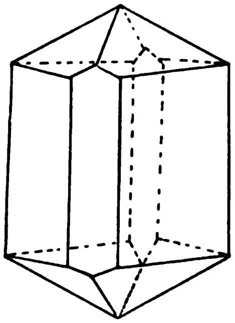
FIG. 190.



Axes of the *rhombic* system.

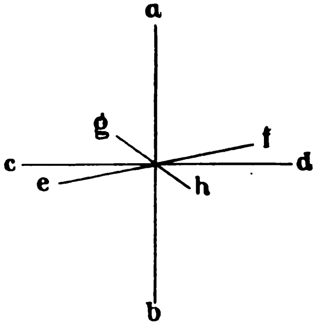
4. *The Hexagonal or Rhombohedral System.* Crystals of th— system have four axes three of which are of equal length and a— called secondary axes, whilst the fourth, known as the primar is either longer or shorter than the other three. The primar is at right angles to the plane of the secondary axes, which in each other at acute angles (see Fig. 193).

FIG. 192.



Rhombic prism.

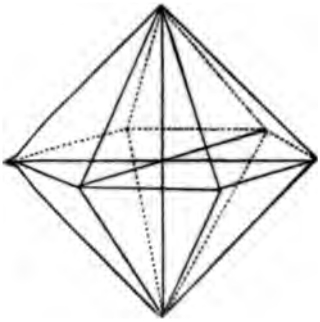
FIG. 193.



Axes of the *hexagonal* system.

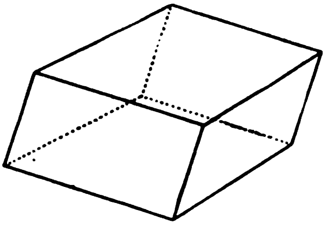
The fundamental form is the double six-sided pyramid (Fig. 194). The rhombohedron (Fig. 195) and the regular six-sided prism (Fig. 196) are modifications of this system.

Fig. 194.



Double six-sided pyramid.

Fig. 195.



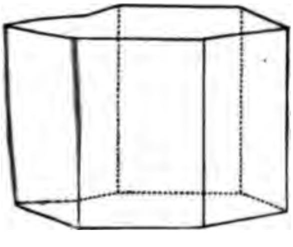
Rhombohedron.

Sodium nitrate, camphor, graphite, ammonium chloride, ice, calcspar, thymol, metallic bismuth and antimony, arsenic, silicic acid, etc., crystallize in this system.

5. The *Monoclinic System*, also known as the Monosymmetric, Clinorhombic, or Oblique Prismatic System.

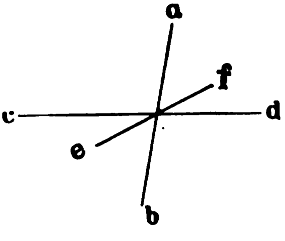
Crystals of this system have three unequal axes, two being obliquely inclined to each other, the other axis forming right angles with these two (see Fig. 197).

Fig. 196.



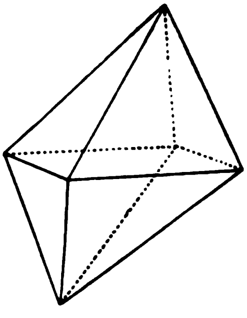
Six-sided prism.

Fig. 197.



Axes of the *monoclinic* system.

Fig. 198.



Monoclinic double pyramid.

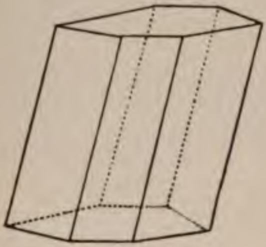
The fundamental forms of this system are the monoclinic double pyramid or octahedron (Fig. 198), and the monoclinic prism (Fig. 199).

Ferrous sulphate, borax, lead acetate, cupric acetate, tartaric acid, potassium chlorate, and sodium acetate, sulphate, thiosulphate, phosphate, and carbonate crystallize in this system.

6. The *Triclinic System*, also known as the Asymmetric, Clinorhombohedral, or Doubly Oblique Prismatic System.

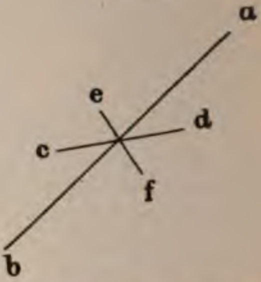
This is the least regular of all the systems, the crystals having unequal axes, all obliquely inclined to one another (see Fig. 200).

FIG. 199.



Monoclinic prism.

FIG. 200.



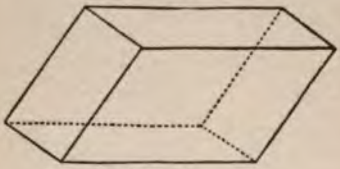
Axes of the *triclinic* system.

The fundamental forms of this system are the triclinic prism (Fig. 201) and the triclinic octahedron or double pyramid (Fig. 202).

Cupric sulphate, potassium dichromate, gypsum, boric acid, manganous sulphate, etc., crystallize in this system.

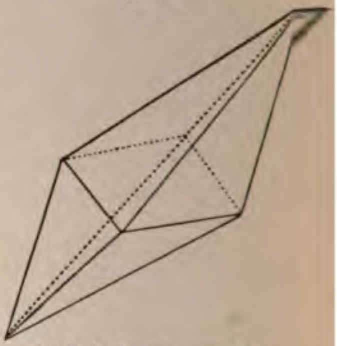
The pyramidal form of crystals is found in all the systems above described, while the cube is confined to the regular system, and prisms are met in all but the regular system. The proper classification of a crystal may be determined by measurement of the angles and subsequent calculation of the length and inclination of the axes; the instrument used for this purpose is known as a goniometer.

FIG. 201.



Triclinic prism.

FIG. 202.



Triclinic double pyramid.

Various methods are employed for obtaining crystals, dependent upon the nature of the substance to be crystallized: thus, by sublimation; by deposition from supersaturated solutions as they cool; by deposition from solutions during slow evaporation of the solvent; by precipitation; by fusion and partial cooling; by the action of a galvanic current upon a solution; and by the addition of a substance having a strong affinity for the solvent, thereby withdrawing it from the solution. The method generally followed is the gradual separation from supersaturated solutions as they cool; if a solution of saline matter made with aid of heat is allowed to cool slowly, the water will gradually evaporate, and in some cases a part of it will unite intimately with the soluble substance to form crystals. Water which is thus appropriated, and which is essential to the constitution of the crystals, is called *water of crystallization;* it varies greatly for different substances, ranging from 5 to 60 per cent. of the weight of the crystals. Crystalline bodies in which this water is entirely absent are said to be anhydrous. Some salts combine with various proportions of water of crystallization according to the temperature at which crystallization takes place, the crystals assuming different forms according to the amount of water taken up; sodium carbonate, sodium phosphate, and zinc sulphate are examples of this class.

Some crystals will part with a portion of their water of crystallization when exposed to the air, particularly if the latter is slightly warm; they gradually lose their transparency and the surface becomes opaque from the separation of dry powder. This change is termed *efflorescence*, and is frequently observed in Epsom salt, sodium carbonate, and borax. Other crystals are inclined to absorb moisture from the atmosphere, and in some instances to such an extent as even to liquefy; the terms *hygroscopicity* and *deliquescence* are used to designate this peculiar property, the latter applying to the more aggravated form. Potassium hypophosphite, zinc chloride and iodide, potassium acetate and carbonate, and lithium bromide are examples of deliquescent crystals. As a rule, crystals containing water of crystallization do not absorb moisture from the air, although calcium chloride, potassium citrate, and sodium hypophosphite are marked exceptions.

Besides the water needed for crystallization, some is also at times mechanically retained within the crystal during the formation of the latter, and is violently expelled upon application of heat; such water is called *interstitial water*, because it fills small interstices or spaces in the crystal, and *water of decrepitation*, because it causes the crystals to decrepitate or crackle when heated, due to slight explosions caused by the escape of aqueous vapor from a confined space. It is impossible to crystallize by a single operation all of the substance held in solution—a portion will remain in solution in some of the water, and this liquid constitutes the *mother-liquor*, which also retains the more soluble impurities. By further concentration the mother-liquor may be made to yield additional crops of crystals.

The time necessary to complete crystallization will vary with the nature of the dissolved body; the end may be assumed to have been reached when the solution has attained the temperature of the surrounding atmosphere, and the time for this must vary, since the dissolved body, by again taking on the solid form, is continually giving out latent heat to the surrounding solution, and thus the actual cooling is retarded. For small quantities and not very soluble substances twenty-four to thirty-six hours should be allowed, while large volumes of solution of readily soluble matter will require from three to six or eight days.

In order to obtain large and well-formed crystals the solution should not be made too concentrated, and should be carefully filtered to obtain a perfectly clear liquid, which should be allowed to remain undisturbed and protected against dust, in a moderate temperature; it is the very slow evaporation of the solvent that enables the particles of dissolved matter to arrange themselves harmoniously and symmetrically around the centre of the crystal forming. Perfect rest is equally essential, as agitation of the crystallizing solution tends to disturb the gradual uniform deposit and causes the formation of small and imperfect crystals, as in the case of commercial magnesium sulphate, zinc sulphate, etc.

The proper degree of concentration of the solution must be determined by the solubility of the substance to be crystallized. If the substance is only moderately soluble, the solution may be evaporated until a crystalline crust or pellicle begins to form on the top of the liquid; but in the case of very soluble substances such a degree of concentration would be too great, and a better plan is to evaporate the solution until a small portion transferred to a glass plate crystallizes within a reasonable length of time. In large operations the manufacturer relies upon the density of the solution as indicated by the hydrometer, and evaporation is continued to such a point as experience has taught to be most desirable for perfect crystallization.

The vessels best adapted for crystallization are deep rough-glazed stoneware basins, called crystallizers, frequently arranged with a lip to facilitate decantation of the mother-liquor; wooden vats are also extensively employed by manufacturing chemists, and in some cases these are lined with lead. For very small operations glass or porcelain dishes may be employed, but their smooth surface is not favorable to the deposit of crystals.

Crystallization is often facilitated by placing insoluble foreign substances in the solution, which form starting-points or nuclei for the process, and to which the crystallizing substance readily attaches itself; pieces of string, wire, wood, etc., may be used for the purpose. Sugar is thus crystallized in the form of rock-candy, by stretching strings transversely across the boxes and tubs into which the syrup is poured.

Since crystals do not increase in size from within, as do animals and plants, but grow from without, by deposition of solid matter upon their surface, it is possible to procure large and well-formed crystals, for specimen purposes, by suspending a crystal in a saturated solution of its own constituent matter. This proceeding may be termed *nursing* a crystal. Isomorphous crystals are capable of growing in each other's solution; hence if a crystal of potassium alum be suspended in a solution of ferric alum or chrome alum, the latter will be found uniformly deposited, and thus a complete envelope of chrome or ferric alum will grow on the original crystal of potassium alum.

CHAPTER XII.

CLASSIFICATION OF THE NATURAL PRODUCTS USED IN PHARMACY.

PLANTS, either spontaneously or after subjection to various processes, yield certain vegetable substances which are extensively employed in pharmacy, and which, owing to their different characteristics as to composition, solubility, etc., have been divided into distinct classes, thus: gums, resins, oleoresins, gum-resins, balsams, fats, volatile oils, etc. Unfortunately the names which from long usage have been applied to some drugs are not in all cases indicative of their nature; hence a knowledge of the characteristic properties of each class of plant products is essential to guard against errors in nomenclature, which are of daily occurrence in commercial transactions; for instance, the names *balsam of fir* and *balsam copaiba* are applied to substances belonging to the class of oleoresins, and not containing any of the principles which characterize the balsams; *gum guaiac* and *gum mastiche* are true resins; *gum benzoin* belongs to the class of balsams; and *gum opium* is an inspissated juice of complex composition. None of the four last-named substances possesses any of the properties of the gums.

True gums are amorphous exudations wholly soluble in cold water, which are not affected by iodine, but are precipitated by alcohol and solution of lead subacetate, the latter being a most delicate reagent for the presence of gums. Neutral or normal lead acetate is readily miscible with solutions of the true gums, of which acacia may be taken as a type. A class of substances formerly called gums are now more appropriately known as *mucilages*, because they differ in several respects from true gums; they are not completely soluble in water (cold or hot), but absorb the same, and in some instances swell to a gelatinoid mass. Mucilages are frequently mixed with starch, which is easily detected by the blue color produced upon addition of iodine solution. Tragacanth and the gummy constituents of flaxseed, elm bark, quince seed, etc., belong to the class of mucilages.

Resins are secretory products, in some instances the result of oxidation of volatile oils, and are widely diffused in the vegetable kingdom; they are wholly insoluble in water, except in the presence of caustic alkalies, but are readily soluble in alcohol, ether, and chloroform, and frequently in fixed and volatile oils. Resins are mostly solid and brittle at ordinary temperatures, generally amorphous, readily fusible and inflammable, become negatively electric by friction, decompose before volatilizing, and are precipitated from their solutions by water and acids. Pine resin, mastiche, jalap resin, and guaiac resin are examples of this valuable class of plant products.

Oleoresins occupy a position intermediate between resins proper and volatile oils, and partake of the properties of both classes; their existence confirms the view held as to the formation of some resins in plants, and their consistence varies with the relative proportions of resin and volatile oil. Like the resins proper, oleoresins are insoluble in water, but soluble in alcohol and ether; they possess a marked odor, due to the volatile oil present, which latter can be separated by distillation, leaving the resin as a solid residue. White turpentine is an example of solid oleoresins, and copaiba of liquid oleoresins.

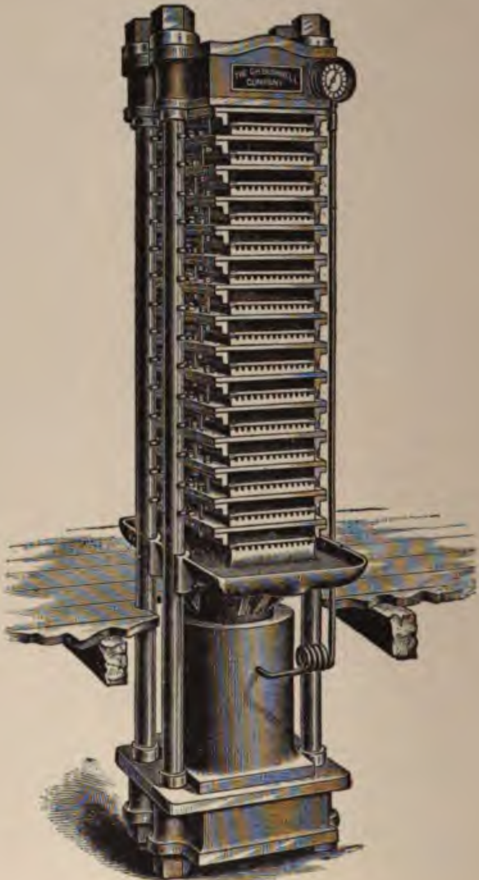
Gum-resins exist in plants in the form of an adhesive milky juice composed of variable mixtures of resin and gum suspended in water; they are obtained as exudations, by wounding the stem or root of the plant and allowing the juice to dry spontaneously. The proportion of gum and resin varies considerably, not only for different gum-resins, but also for different samples of the same gum-resin, and those lots are most valuable which contain the largest amount of resin. The activity of the drug resides wholly in the resin, and this fact is taken into consideration in the official formulas for the tinctures of asafetida and myrrh. A peculiarity of all gum-resins is that when properly triturated with water they yield milk-like mixtures, termed emulsions, which fact is due to the suspension of very finely divided resin in the solution of gum; these milk-like mixtures cannot be obtained if the commercial finely powdered gum-resins be triturated with water, but require the use of the natural product in coarse powder. As prominent gum-resins, may be mentioned asafetida, myrrh, scammony, and ammoniac.

Balsams are either resinous or oleoresinous secretions containing benzoic or cinnamic acid, or both; it is the presence of these acids which distinguishes the balsams from ordinary resins and oleoresins. Balsams are soluble in alcohol, ether, and chloroform, but insoluble in water, although the balsamic principles can be extracted by sublimation or by treatment with hot water. Benzoin and balsam of tolu are examples of resinous balsams, while storax and balsam of Peru belong to the oleoresinous variety.

The fats used in pharmacy are derived mainly from the vegetable kingdom, although a few animal products belonging to the same class are also employed. When liquid at ordinary temperature they are usually designated as fixed oils, although this name is also applied to one vegetable fat, solid and even brittle at 15° C. (59° F.); when strictly pure they are, as a rule, colorless, odorless, and tasteless. Fats proper are of a soft consistence and mostly yield liquid fats when subjected to a gradually increased pressure; those of a firmer consistence are usually termed tallows or suets, and such as are brittle at common temperatures are known as waxes, but these latter are not true fats. The origin of fixed oils in plants is supposed to be the starch, while in animals fats are derived from the carbohydrates and fats consumed. Fats are lighter than water, and insoluble in that liquid; sparingly soluble in cold alcohol, with one or two exceptions; but, as a rule, freely soluble in ether, chloroform, petroleum benzin, carbon disulphide, benzene, etc.; a hot alcoholic solution of fats, in most instances, will deposit them in a crystalline condition upon cooling. All fats, whether liquid or solid, are greasy to the touch, and when dropped upon paper produce a stain which cannot be dissipated by heat; they have boiling-points varying from 260° to 300° C. (500° to 572° F.), and frequently, when thus heated, undergo decomposition and give off acrid, irritating vapors. Fixed oils usually have a specific gravity of from 0.900 to 0.930 at 15° C. (59° F.), though occasionally as high as 0.970, as in the case of castor oil; many oils do not congeal until the temperature has fallen considerably below 0° C. (32° F.), while others deposit solid matter at 10° C. (50° F.). Like water, fixed oils expand upon congealing, and have been known to burst the vessels containing them. Fats are not inflammable, but will burn more or less readily with the aid of a wick. Nearly all vegetable and animal fats consist of a mixture of two or more fats, and when exposed to the air become oxidized, many of them gradually acquiring a disagreeable odor, due to the liberation of odorous fatty acids; this condition is known as *rancidity*, and may be avoided by keeping the fats as free from moisture as possible, in air-tight containers stored in a dry, cool, and dark place. Rancid fats may be improved, and to a certain extent restored, by washing them with warm water, or by treating them with magnesia or other weak alkali, and afterward washing them well. During the oxidation of fats by exposure to air heat is always developed, and certain fabrics, such as woollen and cotton rags, which are known to be poor conductors of heat, are liable to spontaneous ignition if saturated with fats and exposed to the air for some time. Fixed oils may be conveniently divided into *drying* and *non-drying* oils; the former upon exposure to air gradually thicken, and if in thin layers form varnish-like masses, whereas the non-drying oils remain fluid and become rancid.

Although fats are found in various parts of plants, those intended for use are collected exclusively from the fruit and seed, and are obtained either by expression or by extraction with some suitable solvent; the former process yields somewhat lower results, but is preferred because less troublesome and productive in many cases of a superior article. In Fig. 203 is shown an hydraulic press extensively used for the expression of mustard, cottonseed, and linseed oils. The crushed material, after being heated somewhat, is placed in sacks or press-cloths between the series of plates, and pressure applied from below, the oil being collected in the large box o trough, and from there delivered into the receiving vessel. Th residue from certain seed expressions is used, under the name of *oil-cake*, as food for cattle and hogs and for fertilizing purposes. Col expression yields a finer oil than when heat is employed, although slight warming is generally resorted to so as to render the oil more fluid in the seed and thus insure a better flow. Expressed oils are always more or less contaminated with impurities, such as mucilaginous and albuminous matters, which are removed by allowing the oil to settle in large tanks and drawing off the clear liquid. Fre-

FIG. 203.



Steam press for fixed oils.

quently filtration is employed for improving the quality of the oil, felt or flannel bags being best adapted for this purpose. When purification of fixed oils becomes necessary, they are treated either with sulphuric acid, caustic alkalies, zinc chloride, tannin, or alkali carbonates, and subsequently washed with hot water, after which they are carefully decanted.

The extraction of fixed oils is conducted in specially constructed extractors, frequently so arranged that the solvent is made to act upon successive portions of crushed seed, the saturated solution of fat being then transferred to a suitable distilling apparatus, where the solvent is recovered, to be used again for subsequent operations. The solvents usually employed are petroleum benzin of low boiling-point and carbon disulphide; the oil is obtained in larger quantity than by expression, and is free from many impurities often found in expressed oils.

Fixed oils are frequently subjected to a bleaching process, which consists in treating the oil with solution of hydrogen dioxide, potassium permanganate, potassium dichromate, chlorine, or sulphurous acid; of these methods, the hydrogen dioxide process is preferable, as it is least liable to injure the oil, while the use of other bleaching agents necessitates repeated washing of the oil with water and even weak alkali solutions to remove acid oxidation products.

The adulteration of fixed oils is effected by mixing the finer and more valuable oils with inferior and cheaper varieties, and as the crude methods of former years are no longer practised, a better knowledge of the chemical behavior of fats and fixed oils is necessary at the present day. Caustic and carbonated alkalies are practically without effect upon fats and fixed oils in the cold unless free acids, due to rancidity, be present; a more or less uniform mixture results, but no chemical change is produced. If boiled together with solutions of alkali hydroxide or carbonate, all fats and fixed oils used in pharmacy, with the exception of lanolin, wax, and spermaceti, readily undergo saponification and form water-soluble compounds, known as soaps, glycerin being liberated at the same time.

Drying oils may be distinguished from non-drying oils by their behavior with sulphuric and nitrous acids. If 50 Gm. of a fixed oil be mixed with 10 Cc. of concentrated sulphuric acid, heat will be developed varying in intensity for different oils, the drying oils always showing the greatest rise in temperature; thus, while olive oil increases 42 degrees C. in temperature, castor oil 47 degrees C., and oil of almond 52 degrees C., hempseed oil will show a rise of 98 degrees C. and linseed oil 103 degrees C. When mixed with nitrous acid, non-drying oils will gradually be converted into a solid mass, while drying oils remain fluid even after prolonged contact, although a few become somewhat thicker. The test is made by agitating for a short time 1 part of copper foil with 5 parts each of nitric acid and the oil, and setting the mixture aside for about six hours, when solidification is generally completed. Among the prominent non-drying oils are olive oil, castor oil, almond oil, lard oil, sesame or benne oil, croton oil, colza or rapeseed oil, and groundnut oil; while the following belong to the drying oils: linseed oil, cotton-seed oil, poppy-seed oil, hemp-seed oil, and walnut oil.

Animal fats are usually obtained by rendering over a slow fire and then straining to remove the particles of membranous tissue.

The chief use of fats in pharmacy is in the preparation of liniments and ointments, and for this purpose they should be absolutely free from rancidity, and should be preserved in tightly-closed, impervious containers in a cool, dry place.

Of the fats recognized in the Pharmacopœia 7 are of animal origin,—lard, lard oil, cod-liver oil, suet, wool fat, spermaceti, and wax; and an equal number of vegetable origin,—castor oil, cotton-seed oil, croton oil, expressed oil of almond, linseed oil, olive oil, and oil of theobroma.

Lard (Adeps, U. S. P.).—This is the prepared abdominal fat of the hog derived from the so-called leaves, and preferably collected in the winter or early spring, as it has a higher fusing-point than that collected in summer. For pharmaceutical purposes lard entirely free from water should be used; such lard, commercially known as *dehydrated lard*, is prepared by melting leaf-lard with just sufficient water-bath heat and then adding some substance having great affinity for water, but not affecting the lard itself, such as dried calcium sulphate or anhydrous calcium chloride, sodium sulphate, or magnesium chloride. After keeping the melted lard in contact with the dehydrating agent for an hour or more, with frequent stirring, it is carefully strained and then stirred until cool. If much water is present in the lard, a dense liquid layer is likely to be formed in the bottom of the dish if either of the three last-named salts be used, from which the lard can be readily poured off. Dehydrated lard is now manufactured on a large scale, and may be purchased from the leading wholesale druggists at prices but little above the market price of ordinary lard.

Pure lard is liable to become rancid if kept for some time, hence the Pharmacopœia directs its preservation by benzoinating. This is done by suspending 2 parts of coarsely powdered benzoin, contained in loosely textured cloth, for two hours, in 100 parts of melted lard at a temperature not exceeding 60° C. (140° F.), in a covered vessel, then straining and cooling. The balsamic principles of benzoin are soluble in the melted fat, and protect it afterward against change. In summer the preparation, which is officially known as Adeps Benzoinatus, should contain 5 per cent. of white wax, in place of a like quantity of lard, to render it firmer.

Ordinary commercial lard is sometimes found to contain much water, starch, alkalies, and table salt, and occasionally an admixture of cotton-seed oil.

Lard Oil (Oleum Adipis, U. S. P.).—Lard oil is obtained by expression from hog's lard, the yield being about 60 per cent. It is colorless, and when cooled to 10° C. (50° F.) it begins to deposit granular fat. Lard oil is subject to adulteration with cotton-seed oil and paraffin oils.

Cod-liver Oil (Oleum Morrhuæ, U. S. P.).—Medicinal cod-liver oil should always be procured from fresh livers, by the aid of a gradually increased steam heat not exceeding 60° C. (140° F.); the oil is allowed to separate from the watery fluid, and after it has been frozen is expressed in canvas bags, whereby a pure, only slightly colored oil is obtained, the hard yellow residue, consisting of stearin and tissue, being rejected. Cod-liver oil thus prepared keeps well in completely filled vessels, and when cooled to 0° C. (32° F.) should deposit no solid fats; it belongs to the drying oils, and if exposed to the air soon thickens and acquires a disagreeably strong odor and taste. The more probable adulterations of cod-liver oil consist of seal oil and other fish oils, for the presence of which the Pharmacopœia gives appropriate tests.

Suet (Sevum Præparatum, U. S. P.).—The suet officially recognized is that obtained from the abdominal fat of the sheep, and is commonly known as mutton suet. It usually is well washed with water, then melted and strained, but still is accompanied by a peculiar, rather disagreeable odor, from which it can be freed by filtration through paper in a hot-water funnel. Suet turns rancid very readily.

Wool Fat (Adeps Lanæ, U. S. P.).—The wool of sheep contains a natural grease of complex composition, which is readily removed in the process of washing the wool. If this grease be treated with weak alkalies, repeatedly washed with water, and then extracted with acetone, it yields a purified fat of yellowish-brown color and characteristic odor, and having about the same melting-point as lard. This constitutes the official wool fat. It possesses the advantage over other fats of being easily miscible with large quantities of water (twice its weight) without losing its ointment-like character. When mixed with water in the proportion of 3 parts of the latter with 7 parts of wool fat, it constitutes hydrous wool fat, commercially known as lanolin, and recognized in the Pharmacopœia under the title Adeps Lanæ Hydrosus.

Spermaceti (Cetaceum, U. S. P.).—Spermaceti is obtained by expression from the fatty secretion found in the cranial cavity of the sperm whale. Before the animal is killed the fat is liquid, but afterward congeals to a yellow mass; by expression a yellow oil is removed, the residue is melted, washed with weak potassa solution and water, and finally allowed to congeal. Spermaceti is apt to become yellowish and rancid from age and when exposed to air; it melts at about 50° C. (122° F.).

Wax, White and Yellow (Cera Alba; Cera Flava, U. S. P.).—The only wax recognized by the Pharmacopœia is that secreted by bees, and used by them in the construction of the honey-comb. To obtain the wax, the honey is drained from the comb, which is then expressed, melted in water, and, after the impurities have subsided, run into moulds and cooled. This constitutes yellow wax, from which white wax is made by a process of sun-bleaching, as follows: Melted wax is again solidified in the form of thin ribbons or bands by allowing it to flow over wet revolving cylinders; these bands are moistened with water, and exposed to sunlight in the open air. After exposure for some time the color disappears in spots and the wax is again melted, resolidified, and treated as before, the process being repeated until the wax is completely bleached, when it is finally melted and run into moulds; besides losing its color, wax thus treated is somewhat changed by long exposure to light and air, and is more disposed to rancidity than yellow wax, as is noticeable in the modified odor. Pure yellow wax melts at 63° to 64° C. (145.4°–147.2° F.), white wax at 65° C. (149° F.); they differ from true fats in not containing glycerin, and in not forming soap when boiled with solution of alkali carbonates. Wax is completely dissolved by ether and chloroform, but not by boiling alcohol and cold benzene or carbon disulphide. Besides the crude adulterations readily observed in melted wax, tallow and other fats, as well as vegetable wax, resin, and paraffin, are occasionally mixed with it; they can be readily detected by the pharmacopœial tests.

Almond Oil (Oleum Amygdalæ Expressum, U. S. P.).—Expressed oil of almond is commercially better known as oil of sweet almond, although large quantities of the oil are obtained from the bitter almond. The yellowish color of the oil is due entirely to the colored episperm, for if blanched almonds be expressed a colorless oil will be obtained. The oil remains perfectly clear if cooled to —10° C. (14° F.), and does not congeal until a temperature of —20° C. (—4° F.) is reached. It is often adulterated with the expressed oils of apricot and peach kernels, and also other fixed oils, for which the Pharmacopœia gives appropriate tests.

Castor Oil (Oleum Ricini, U. S. P.).—This oil is obtained by expression from the seed of the plant popularly called palma christi, the finest quality being secured by cold expression. It differs from other fixed oils in being soluble in all proportions of absolute alcohol and in 3 times its volume of a mixture of 19 volumes of official alcohol and 1 volume of water. Castor oil is rarely adulterated.

There are at present six mills in this country where castor oil is expressed—one each in Jersey City, N. J.; Kansas City, Mo.; East St. Louis, Ill., and Memphis, Tenn., and two in St. Louis, Mo. The seed, or castor-bean, as it is called, from which the oil is expressed, is produced in the states of Illinois, Kansas, and Missouri, and in Oklahoma Territory, but the chief supply of late years has come from British India. The origin of the name castor oil is somewhat in doubt. The plant, having been introduced into the West Indies shortly after the discovery of this country, was mistaken by the Spaniards for an entirely different plant—the *Vitex angus castus*—and named by them *agno casto*, from which the English coined the word *castor* and probably applied the name to the oil.

Cottonseed Oil (Oleum Gossypii Seminis, U. S. P.).—The official cottonseed oil is refined bleached oil, for the crude product, obtained by hydraulic pressure from the seed, has a brown color and linseed-like odor, and contains considerable quantities of albuminous matter. After subsiding, the crude oil is treated with superheated steam, and finally well shaken with heated weak alkali solution. The yield of oil from cottonseed varies from 12.5 to 20 per cent. It congeals when cooled to 0° or —5° C. (32° or 23° F.), and is instantly colored dark reddish-brown on contact with concentrated sulphuric acid; it belongs to the drying oils, but shaken with nitric acid and water it gradually forms a colored semisolid mass. The chief use of cottonseed oil is as a substitute for more expensive fixed oils, as in the case of some of the official liniments, and there is no doubt that it is extensively employed as an adulterant for almond, olive, and other oils.

Croton Oil (Oleum Tiglii, U. S. P.).—While fresh croton oil requires from 50 to 60 times its weight of alcohol for solution, the solubility increases materially with age. The oil does not congeal until cooled to —16° C. (3.2° F.). Although it belongs to the class of non-drying oils, it remains liquid if vigorously shaken with fuming nitric acid and water and then allowed to stand for 1 or 2 days; this behavior distinguishes croton oil from other non-drying oils and serves to detect adulteration with the latter.

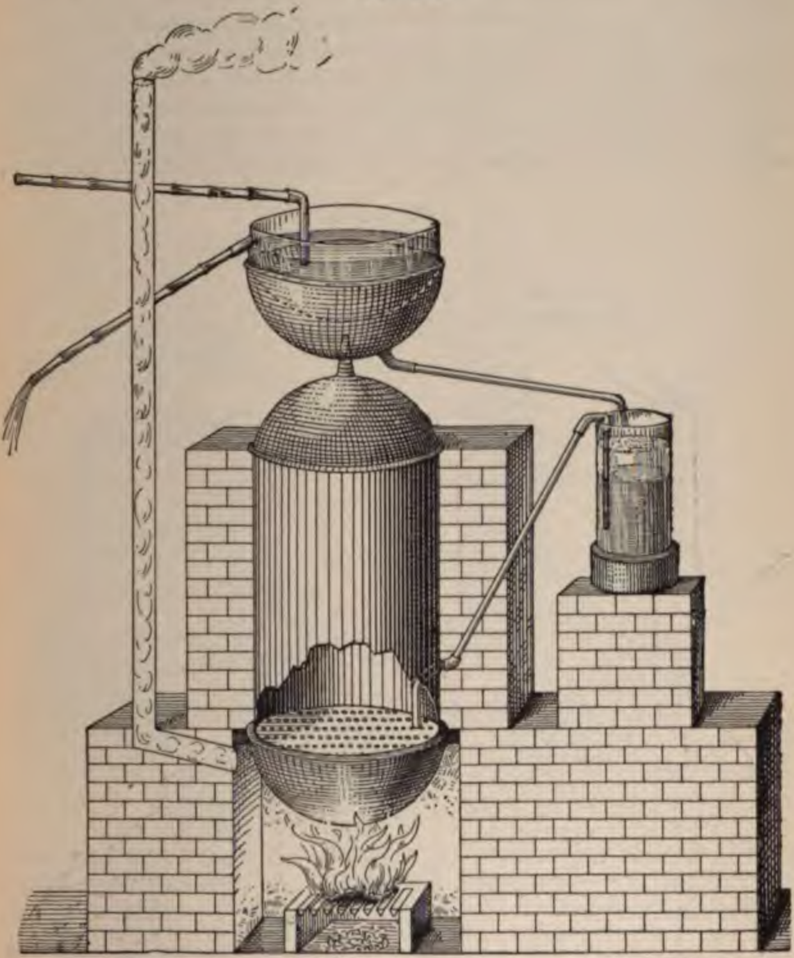
Linseed Oil (Oleum Lini, U. S. P.).—Much of the linseed oil offered is expressed with the aid of heat, as thereby the yield is increased nearly 50 per cent. Like expressed oil of almond, linseed oil does not congeal until cooled to —20° C. (—4° F.). It is soluble in an equal volume of official alcohol, but becomes turbid if the proportion of alcohol is doubled. Linseed oil is one of the best drying oils known. The so-called boiled linseed oil of commerce should never be used in pharmacy.

Olive Oil (Oleum Olivæ, U. S. P.).—Various grades of olive oil are found on the market, the best being that commercially known as Virgin Olive Oil, which is obtained by cold expression from the flesh only of the ripe olive. It is of a pale-yellow or light greenish-yellow color, and becomes cloudy at 10° C. (50° F.), congealing to a whitish, granular mass at 0° C. (32° F.). Much of the olive oil offered for sale is adulterated with cottonseed oil, groundnut oil, or sesame oil.

Oil of Theobroma (Oleum Theobromatis, U. S. P.).—This oil, better known as cacao butter, is the only official fixed oil solid at ordinary temperature. It is obtained to the extent of 40 per cent. by expression between hot plates from the roasted seeds of the cacao tree, which subsequently yield the well-known cacao mass or chocolate. While brittle at 15° C. (59° F.), it melts readily at the temperature of the human body, and for this reason is admirably adapted for use as a vehicle in making suppositories. Cacao butter is subject to adulteration with tallow, stearin, and paraffin, the presence of which can be detected by the low fusing-point and the high congealing-point of the oil.

Volatile oils are mixtures of those substances to which, in a majority of cases, the peculiar odors of plants are due. Although the attribute volatile is indicative merely of a physical property which most of these substances have in common, and in nowise refers to their source, the designation volatile oil has been restricted entirely to volatile products from the vegetable kingdom. In recent years the term has been made to include artificial substances identical with, or at least closely related to, such natural plant products. Volatile oils do not all preëxist in the plant, some being the result of fermentative action between certain constituents of the plant in the presence of water, and others being produced by destructive distillation. Volatile oils may exist in every part of the plant from the root to the seed, and when several oils are present in different parts of the same plant they will generally be found to differ in physical as well as chemical properties; as, for instance, the oils of orange obtained from the leaf, flower, and rind. Volatile oils usually occur in separate cells, as glands in the herbaceous portion and rinds of many fruits, or distributed throughout the interior tissue, or forming distinct oil tubes, as in the fruit of fennel, anise, etc. The odor of volatile oils, while in some instances due to their particular composition, in others appears to be due to atmospheric influences, since oil of turpentine and other oils when rectified in an atmosphere of carbon dioxide have been found devoid of all unpleasant odor, and yet, when again exposed to the air, they soon acquired their characteristic odor. With few exceptions, volatile oils are lighter than water, and their solubility in water is very variable; their specific gravities at 25° C. (77° F.) range from 0.845 to 1.180. Absolutely pure volatile oils are colorless, but the commercial varieties are frequently colored yellow, green, blue, red, and brown; the color in most instances disappears when the oil is brought into solution. Many volatile oils are completely soluble in glacial acetic acid, and all are soluble in alcohol, but in proportions varying from less than an equal volume to ten or more. They have but few properties in common with fixed oils, but like these are soluble in ether, chloroform, and carbon disulphide. Freshly prepared volatile oils are generally freely soluble in benzin, but after exposure they gradually lose this property, and often form turbid mixtures when shaken with the same. When dropped upon filtering paper they cause a stain somewhat resembling that of fixed oils, but which is dissipated upon the application of heat; the stain produced by old or partly resinified volatile oils frequently cannot be removed by heat, but can be readily distinguished from the stain of fixed oils by its shining, varnish-like appearance and by its complete removal with the aid of warm alcohol, the stain from fixed oils being devoid of lustre and insoluble in alcohol. Volatile oils are inflammable, and burn with a bright but sooty flame; exposed to air and light they are more or less rapidly oxidized, being gradually converted into a viscid oil, and finally even into a solid resin. They never become rancid in the sense mentioned under fixed oils, and do not contain glycerin. Owing to the changes which volatile oils undergo through exposure to light and air, they should be preserved in well-stoppered bottles in a dark place; amber- or yellow-colored glass is best adapted for oil containers, as it intercepts the actinic rays of light. The addition of deodorized alcohol or Cologne spirit will also preserve the fine aroma of such oils as lemon and orange, not more than 5 per cent. by volume being necessary. Resinified oils may be restored by redistillation with water or weak alkali, or, if in small quantities, by Cuvier's method, which consists in shaking the oil for fifteen or twenty minutes with a magma formed of animal charcoal and a solution of borax, whereby the resinified portion is

Fig. 204.

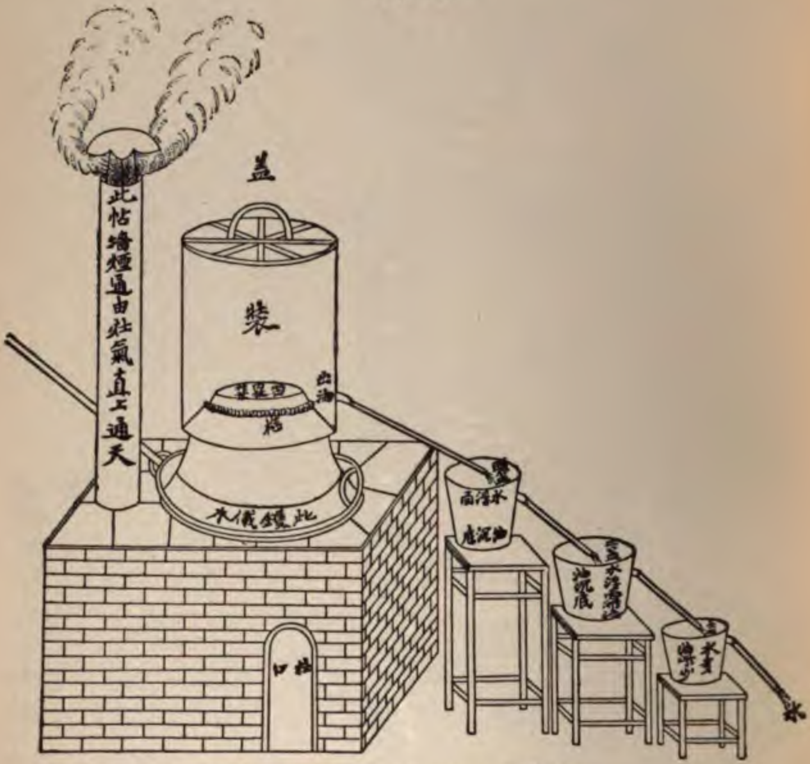


Distillation of oil of star-anise in Tonquin, Asia.

united to the borax and the oil becomes limpid. The whitening of corks in bottles containing volatile oils is due to the presence of ozone produced by the gradual oxidation of the oil.

The adulterations to which volatile oils are subjected are fixed oils, alcohol, and highly rectified petroleum; frequently, also, the higher-priced oils are mixed with cheaper and inferior oils. Fixed oils are easily detected by a permanent greasy stain upon paper, and by a non-volatile residue when the suspected oil is subjected to distillation. Alcohol may be tested for in several ways. If the oil be shaken in a graduated tube with an equal volume of water or glycerin, and then allowed to stand at rest, any diminution in the volume of the oil would indicate alcohol, and approximately also the proportion present; if considerable alcohol be present, the characteristic lambent blue flame of burning alcohol will be observed if a portion of the suspected oil is ignited in a dark room; fused calcium chloride and dry potassium acetate are insoluble in volatile oils, but in the presence of alcohol become soft and even liquid, depending upon the proportion of alcohol; potassium acetate and

FIG. 205.

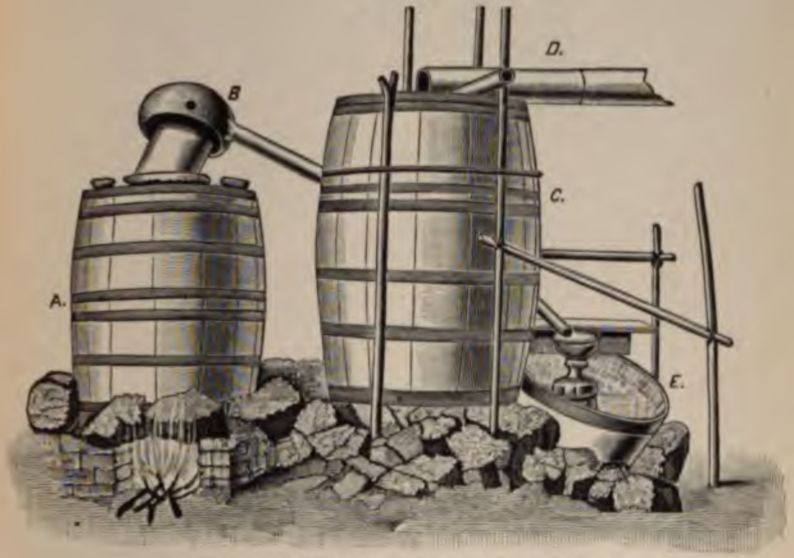


Distillation of oil of cinnamon in China.

sulphuric acid added to volatile oils will generate acetic ether if alcohol be present, which may be detected by its odor; and aniline-red is insoluble in pure volatile oils, but colors these red in the presence of alcohol. Adulterations with rectified petroleum are often not easily detected, and may require a careful chemical examination; for it, as well as for the inferior volatile oils, the Pharmacopœia prescribes appropriate tests under the head of the respective oils likely to be thus contaminated.

The usual method of obtaining volatile oils is by distillation. In some of the Asiatic countries, where the world's supply of a few volatile oils is still obtained, rather crude methods prevail even at the present time. Thus the plan is followed of using wooden cylindrical stills provided with a perforated diaphragm or false bottom, as shown in Fig. 204, on which the oil-yielding material is placed, water being put into the boiler on which the still rests and direct heat applied until the water boils, and the boiling continued as long as the distillate shows the presence of volatile oil. As shown in the illustration, the vapors are condensed in the cup-shaped condenser above the still, and flow from there into a suitable receiver, made of wood and lined with tin, whence the watery portion of the distillate flows back into the still, while the oil rises to the surface and is removed when a sufficient quantity has collected. In Fig. 205 may be seen the peculiar arrangement of a wooden still with tin condenser for the distillation of oil of cassia cinnamon. The still, as in the preceding case, is provided with a perforated bottom and rests upon an

FIG. 206.



Distillation of oil of cajuput in the Molucca Islands.

iron boiler placed directly over the firepot of a brick furnace. The distillate collects in a gutter near the bottom of the cylindrical condenser and flows from there into earthenware receivers. Oil of cinnamon being heavier than water, the distillate is collected in a series of vessels in which the oil sinks to the bottom and the aqueous

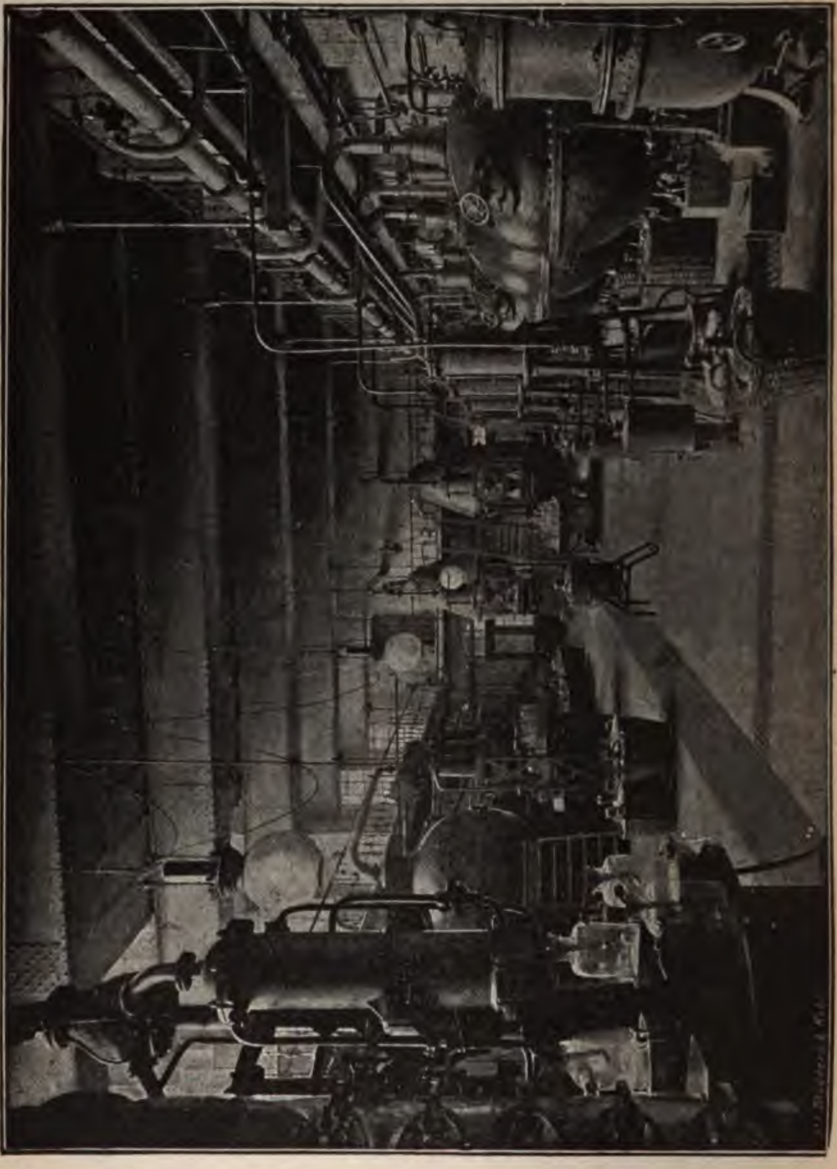


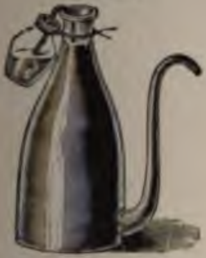
Fig. 207.

Modern distillation of volatile oils by steam.

portion flows into another vessel, to be again used in a subsequent distillation. A still cruder apparatus, in use as recently as 1894, is shown in Fig. 206. It is used for the distillation of oil of cajuput, and consists of a wooden cask, *a*, into which are placed the leaves of the melaleuca plant and some water, and which is heated by means of a rudely constructed fireplace. The vapors are carried through the tin still-head *b* by means of a tube into the second cask *c*, which is kept supplied with cold water running in through the tube *d*, made of bamboo, where they are condensed and flow through a funnel-shaped device, made of cocoanut shell, into a bottle. The oil and water gradually separate, the oil rising to the surface and the water flowing into the tub *e* through a small hole near the bottom of the bottle.

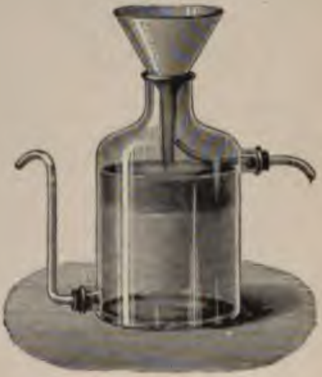
Although the boiling-points of volatile oils are considerably above that of water, the oils pass over rapidly with the vapor of boiling water, and in the leading establishments in this country and Europe volatile oils are now distilled by passing steam under pressure into stills which contain the material on a series of perforated trays extending across the inner body of the still; by this method compaction is avoided, the steam can readily penetrate every particle of the material, and a much finer quality of oil results, since prolonged contact with boiling water has a deleterious effect upon many oils. Fig. 207 represents the interior of a modern establishment for the distillation of volatile oils by steam, as carried on by Messrs. Schimmel & Co., at Leipzig, Germany, to whom the author is indebted for the loan of this and other illustrations shown in this chapter. Whenever the volatile oil is deeply imbedded in the material, as in the case of cloves, cubebs, and many barks and seeds, it is necessary that this first be reduced to a coarse powder so as to facilitate the liberation of the oil. The distillate, which is a mixt-

FIG. 208.



Florentine flask for collecting volatile oils.

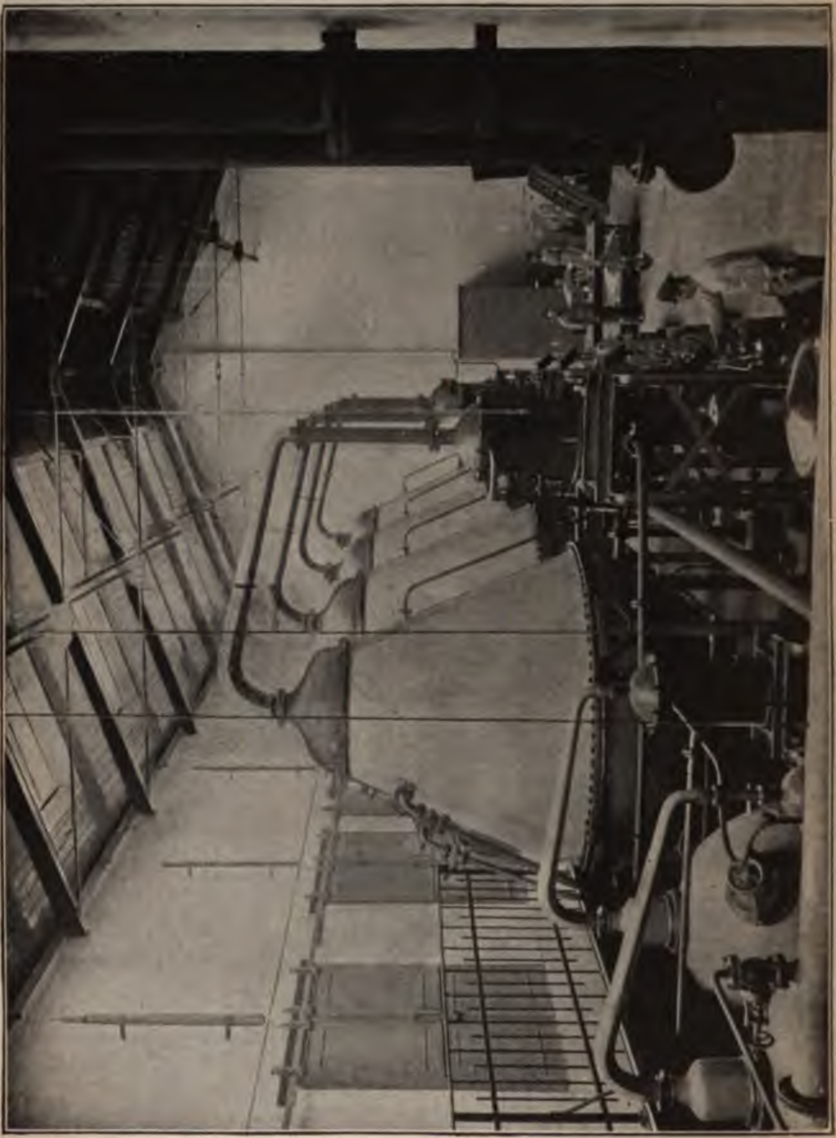
FIG. 209.



Receiver for volatile oils with two outlets.

ure of oil and water, is collected in suitable receivers, either in the form of Florentine flasks with a single outlet tube near the bottom and reaching nearly to the top, as shown in Fig. 208, or of tall cylinders provided with two tubes, a long one near the bottom and a short one near the top; as the distillate cools, it separates into two distinct layers, one consisting of pure oil and the other of water

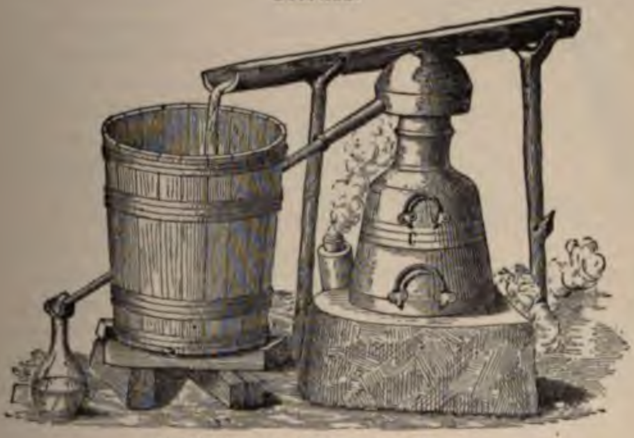
FIG. 210.



Modern apparatus for the distillation of oil of rose.

holding some oil in solution and suspension, which is subsequently regained, either by conveying the water back direct to the still or by distilling the water in separate stills, frequently after the addition of table salt to facilitate separation of the oil. As a rule, the layer of oil floats on top, except in those cases in which the oil has a specific gravity above 1.000, as the oils of cloves, cassia, gaultheria, etc. The lower layer will flow off through the long tube as soon as the liquid in the flask or cylinder reaches the height of the curve in the tube, and will continue to flow as long as distillation continues. When the upper layer fills the vessel, the latter must be changed; or if it is provided with two tubes, as shown in Fig. 209, the liquid will pass out through the short tube into another receptacle; thus the two layers of liquid are withdrawn simultaneously almost as fast as separation takes place.

FIG. 211.



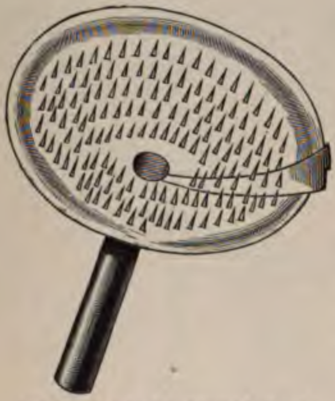
Distillation of oil of rose in Bulgaria.

The contrast between modern distillation of volatile oils by steam and former crude methods still practised in some countries, is strikingly shown in the two illustrations representing the distillation of oil of rose. Fig. 210 represents a complete steam plant for distillation of the oil, at Leipzig, Germany, from flowers grown in the near-by districts. In Fig. 211 is shown the arrangement of a copper still extensively used by the Bulgarians at the present time, which is capable of accommodating a charge of about 22 pounds of freshly gathered roses and 20 gallons of water.

Besides distillation, other methods are employed for obtaining volatile oils, such as expression by hand or machine, and extraction by means of suitable solvents; for certain flowers possessing delicate fragrance, such as the violet, heliotrope, mignonette, tuberose, etc., which do not contain volatile oils in appreciable quantities, the treatment with fats by maceration and digestion, or the pneumatic process, is resorted to for obtaining the odorous principles.

Expression is particularly suited for those oils contained in the epidermal cells of the fruit, as in the natural order Aurantiaceæ, and yields oils of superior quality; the oils of orange and lemon are very sensitive to heat; and hand-pressed oils always command a higher price on account of their delicate aroma. A special apparatus, known as *écuelle à piquer* (a pricking basin) (see Fig. 212), is extensively employed in Southern France; it consists of a tin basin about 8 inches in diameter, studded with numerous (150) short, pointed brass needles, and provided with a hollow handle. The operator holds the basin in one hand and with the other, while rotating the fruit, he continually presses it against the needle-points, thus rupturing the oil-cells and causing the oil to flow into the handle, whence it is transferred to larger vessels and allowed to separate from any fruit juice with which it has become contaminated. Another method of hand-pressing is practised in Italy, known as the sponge method; the rind of the fruit is separated from the pulp and cut into three or four strips, which are held over a sponge and expressed by convex flexion, whereby the cells are burst and the oil is ejected. When the sponge has become saturated with oil it is expressed into an earthen vessel. The residual rind is frequently mixed with water and again expressed in linen sacks, to yield a lower grade of oil.

FIG. 212.



Pricking basin for obtaining hand-pressed volatile oils.

The solvents employed for the extraction of volatile oils are petroleum benzin, ether, carbon disulphide, acetone, etc., solution being effected in tightly closed apparatus by means of maceration and percolation. After complete extraction of the volatile oil the solvent is recovered by distillation at temperatures not affecting the oil, and the residue must then be further purified by rectification. The chief drawback to this method is the possible extraction of other substances besides volatile oils, such as resin, fat, etc., which are sometimes eliminated with great difficulty; hence it is not employed to any great extent.

The process of maceration is confined to the extraction of delicate odors from flowers, and belongs more properly to the art of perfumery than to pharmacy; although the odors are quite marked and persistent, the volatile oil in many flowers is present in such small quantity that it cannot be recovered by distillation, and in some cases is injured by even moderate heat. Complete absorption of the odorous principle by fats in the cold is practised on a large scale in

France, where the process is known as *enfleurage;* bland, inodorous fats, such as purified lard, tallow, olive oil, benne oil, and cottonseed oil, being used for the purpose. In the last three cases the flowers are left in contact with the oil in closed vessels for some time and then strained. When solid fats are used, they are spread thinly on plates of glass, and then covered with flowers, which are renewed from time to time as long as the fat continues to absorb the odor. The fats, impregnated with the odor of the flowers, are finally scraped from the glass, and constitute the well-known French pomades so extensively employed in the manufacture of fine perfumery. In order to extract the odor, the pomade is repeatedly shaken (washed) with deodorized alcohol, and the solution exposed to cold in special cylinders, called crystallizers, whereby all trace of fat is removed.

The pneumatic method consists in passing a current of air into a vessel filled with fresh flowers, whereby the air becomes laden with perfume, and is then passed into another vessel containing fat in a fine state of division, so that intimate contact between the air and fat is effected, and thus the odor is transferred to the fat.

Very few volatile oils are of simple composition, and some are known to contain even six or eight distinct bodies. While formerly many arbitrary and erroneous notions were entertained regarding the nature of volatile oils, much light has been shed upon their true character by Wallach and others during the past twenty or twenty-five years.

Volatile oils may be conveniently divided into groups for the purpose of facilitating classification and better study of general properties. Thus, Group 1 comprises the simple hydrocarbon oils, and to this group the name terpenes is generally applied; Group 2 comprises oils composed of variable mixtures of hydrocarbons and their oxygen derivatives, a few of the oils even consisting entirely, or very nearly so, of such oxygen compounds; Group 3 embraces a small number of oils characterized by the presence of sulphur derivatives; Group 4 comprises the empyreumatic oils, or those obtained by destructive distillation.

The chemical character and composition of volatile oils will be considered further on, when the student's knowledge of chemistry will better fit him for a proper understanding of the subject.

Group 1.—The hydrocarbon oils are the simplest volatile oils known, being composed of carbon and hydrogen only, and are derived mainly from the natural orders Coniferæ, Leguminosæ, and Piperaceæ. They are divided into hemiterpenes, terpenes, sesquiterpenes, diterpenes, etc. Some of these are frequently found present also in members of the other groups. The terpenes proper occur in five isomeric forms (having the same centesimal composition, but different properties), known as *pinene*, *dipentene*, *limonene*, *sylvestrene*, and *phellandrene;* of these, sometimes two or three are found associated in the same oil. As a class, the hydrocarbon oils are the least soluble in alcohol and water, and have specific gravities ranging from 0.850 to 0.900. They readily become resinified when exposed to the air, and when left in contact with alcohol and nitric acid gradually absorb water and yield crystallizable compounds. They react violently with iodine, and are converted into a hard resinous mass by nitric acid.

The official members of this class are oil of copaiba, oil of cubeb, oil of erigeron, oil of juniper, and oil of turpentine.

Group 2.—These oils, as stated above, contain oxygen compounds, and are composed of variable mixtures of terpenes and other bodies, such as alcohols, aldehydes, ethers, acids, ketones, phenols, etc., which can be separated by fractional distillation. They are widely diffused in plants; the larger number are derived from the natural orders Umbelliferæ, Labiatæ, Lauraceæ, Myrtaceæ, and Compositæ. The majority of oils belonging to this group are soluble in an equal volume of alcohol or glacial acetic acid, and many are soluble in these two liquids in all proportions. They are far more soluble in water than are the simple terpenes, and hence are largely used in the preparation of medicated waters. Decreased solubility in alcohol, or in a mixture of alcohol and water, is frequently made a test for adulteration with hydrocarbons and other oils.

While nearly all the oils containing oxygen derivatives of the hydrocarbons are lighter than water, a few will sink when dropped into water, the highest specific gravity for volatile oils being found in this class, namely, 1.180 at 25° C. (77° F.) Some, owing to their peculiar chemical composition, form a solid mass when shaken with an equal volume of concentrated potassa or soda solution, while others show a similar reaction with sodium bisulphite. Upon exposure to low temperatures some of the oils of this class thicken, and even congeal to a solid mass, which property is utilized as a test for their quality. The value of these oils lies, as a rule, in the oxygen compounds which they contain, and which are present in the different oils in proportions varying from 3 to 90 per cent. and over. By producing these synthetically, artificial oils, identical with the natural, have been made, of which the official methyl salicylate or artificial oil of wintergreen (identical also with the natural oil of sweet birch) is an example. The Pharmacopœia recognizes a single concrete volatile oil—camphor—which has been appropriately placed among the oils of this group, since its chemical composition shows it to be a ketone.

The official members of Group 2 are the oils of anise, bergamot, betula, cajuput, caraway, cloves, chenopodium, cinnamon, coriander, eucalyptus, fennel, gaultheria, hedeoma, lavender flowers, lemon, orange flowers, orange peel, peppermint, spearmint, nutmeg, pimenta, rose, rosemary, santal, sassafras, savin, and thyme.

Some plants do not produce volatile oils in nature, but contain certain principles which, in the presence of water, react upon each other, causing the formation of new compounds, one of which is a volatile oil; such is the case with certain plants belonging to the natural order Rosaceæ, suborder Amygdalæ. The name nitrogenated oils was formerly given to this class because in their formation they are always accompanied by a substance containing nitrogen, hydrocyanic acid, which is present in variable proportion and which gives to the oils their poisonous character. The only official oil belonging to this subclass is the oil of bitter almond, which is prepared by mixing freshly powdered bitter almonds with the residue left after expressing the fixed oil from bitter and sweet almonds, adding water, and distilling at a moderate heat. The specific gravity of the oil ranges from 1.045 to 1.060 at 25° C. (77° F.), and that of the purified oil is about 1.032. The oil is sometimes adulterated with nitrobenzene or artificial oil made from toluene. Bitter almonds, as well as peach and apricot seeds, contain both the albuminous ferment and the peculiar compound, amygdalin, necessary for the reaction; while sweet almonds contain only the ferment, and hence will yield no volatile oil unless mixed with the bitter variety. The bulk of "oil of bitter almond" is no doubt now obtained from apricot and peach seeds. The hydrocyanic acid present in oil of bitter almond sometimes amounts to as much as 6 or 7 per cent., and may be removed by shaking the oil with ferrous chloride and lime-water and then rectifying by distillation. Oil of bitter almond is soluble in 300 parts of water and in all proportions of alcohol.

Group 3.—The oils belonging to this group, as in the preceding group, are the result of fermentative action, in which the living plant takes no part except to provide the necessary active principles for the subsequent reaction in the presence of water. Sulphur is present in the oils, combined with certain organic radicles, in the form of sulphide or sulphocyanate. Nearly all the oils of this class are obtained from members of the natural order Cruciferæ. The Pharmacopœia recognizes but one volatile oil containing sulphur, namely, the volatile oil of mustard, made from black mustard seed, which has a specific gravity varying from 1.013 to 1.020 at 25° C. (77° F.).

Group 4.—Among the products of destructive distillation are certain volatile oils which are characterized by a peculiar tarry odor, and acid reaction and a somewhat bitter taste, and known as empyreumatic oils. They are lighter than water, and sparingly soluble in this liquid, but readily soluble in alcohol. Oil of cade and oil of tar are the only empyreumatic oils recognized in the Pharmacopœia; the former is obtained by the dry distillation of the wood of the prickly cedar (Juniperus oxycedrus) and the latter by distillation of tar.

PART II.

PRACTICAL PHARMACY.

THE study of practical pharmacy involves both galenical and extemporaneous pharmacy, the former pertaining to the various preparations of drugs, the later to the many operations of the dispensing counter. The different classes of plant products used in medicine, as well as the various methods of solution and separation, have been considered in previous chapters; the numerous preparations of drugs will be treated after a plan which, for a number of years, has proved satisfactory to students, and although not based on a strictly symmetrical arrangement, is probably in keeping with the advance made by them in other branches of study up to this point.

The official preparations may be divided into those of a strictly pharmaceutical character and those involving chemical action; the latter class will be considered under the head of pharmaceutical chemistry, where the preparations of each element or compound will be grouped together.

The galenical preparations of the Pharmacopœia may be classified as follows: 1. Waters; 2. Solutions or Liquors; 3. Decoctions and Infusions; 4. Syrups; 5. Mucilages, Honeys, and Glycerites; 6. Elixirs; 7. Spirits; 8. Tinctures; 9. Wines and Vinegars; 10. Fluid Extracts; 11. Extracts; 12. Oleoresins and Resins; 13. Collodions; 14. Emulsions; 15. Mixtures; 16. Pills; 17. Lozenges and Confections; 18. Powders and Triturations; 19. Granular Effervescent Salts; 20. Cerates and Ointments; 21. Liniments and Oleates; 22. Plasters and Suppositories.

The operations of the dispensing counter are intimately associated with the various preparations of drugs officially recognized, and, instead of treating them separately under a special head, it has been thought most convenient to consider them in connection with some of the subdivisions named above, particularly as eight classes of the official galenical preparations require remarks and explanations which apply equally to the details of dispensing pharmacy. Certain forms of administering medicines, not as yet recognized in the Pharmacopœia, but which of late years have come into use extensively, such as Compressed Tablets, Tablet Triturates, Hypodermic Tablets, Medicated Disks, etc., may be looked upon as modifications of the official class of lozenges and studied in connection with these.

Official Waters made by Triturating the Medicinal Ingredients with Purified Talc, and then Mixing with Cold Distilled Water and Filtering.

Latin Name.	English Name.	Composition.
Aqua Anisi	Anise Water	2 Cc. of Oil of Anise and 998 Cc. of Distilled Water.
Aqua Camphoræ	Camphor Water	8 Gm. of Camphor in 1000 Cc. of finished product.
Aqua Cinnamomi	Cinnamon Water	2 Cc. of Oil of Cinnamon and 998 Cc. of Distilled Water.
Aqua Fœniculi	Fennel Water	2 Cc. of Oil of Fennel and 998 Cc. of Distilled Water.
Aqua Menthæ Piperitæ	Peppermint Water	2 Cc. of Oil of Peppermint and 998 Cc. of Distilled Water.
Aqua Menthæ Viridis	Spearmint Water	2 Cc. of Oil of Spearmint and 998 Cc. of Distilled Water.

With the exception of camphor water, this whole class is prepared by triturating the oil with about 8 times its weight of purified talc, after which the distilled water is gradually added with continued trituration; the mixture is finally filtered through paper. Thorough trituration with an insoluble powder causes division of the oils into minute particles, in which condition they are more readily dissolved by water. In the case of camphor water, 8 Gm. of camphor are dissolved in 8 Cc. of alcohol, and then triturated with 15 Gm. of purified talc until the alcohol has evaporated, after which the preparation is finished like the others. It is important that the purified talc be not used in the form of an impalpable powder, as this is apt to pass through the filter and necessitate frequent refiltration, but a coarser powder, about No. 60, should be employed. Permission is also given in the Pharmacopœia to effect solution of the volatile oil by replacing the purified talc by pulped or shredded filter-paper, or by the addition of oils to hot water and separation of the excess of the former after active agitation and subsequent cooling of the mixture, or by distillation of the drug or oil with water. When shredded filter-paper is used, the best plan is to drop the oil upon the shredded paper, add this to the hot distilled water contained in a strong bottle or jug, and shake actively until the liquid is cold, after which a perfectly clear solution may be obtained by simple filtration. In the author's experience this method produces excellent results with little labor. The use of alcohol for the purpose of facilitating solution of the oil in the water must be condemned as liable to cause trouble, the very weak alcoholic liquid having a tendency to become sour through oxidation under favorable conditions. Calcium phosphate, directed in the U. S. P., 1890, is not a good medium for division of the oils, and is frequently found impure from contamination with soluble matter. Magnesium carbonate, at one time largely used, is not desirable, as it is not wholly insoluble, and this fact has often given rise to trouble, as in the case of cinnamon-water, which invariably has a yellow color when made with this agent, and in the case of mixtures of medicated waters with lime-water, producing turbidity.

OFFICIAL WATERS MADE BY DISTILLATION.

Latin Name.	English Name.	Strength.
Aqua Aurantii Florum Fortior .	Stronger Orange Flower Water.	Saturated.
Aqua Destillata	Distilled Water	Absolutely pure.
Aqua Hamamelidis	Hamamelis Water	(?)
Aqua Rosæ Fortior	Stronger Rose Water	Saturated.

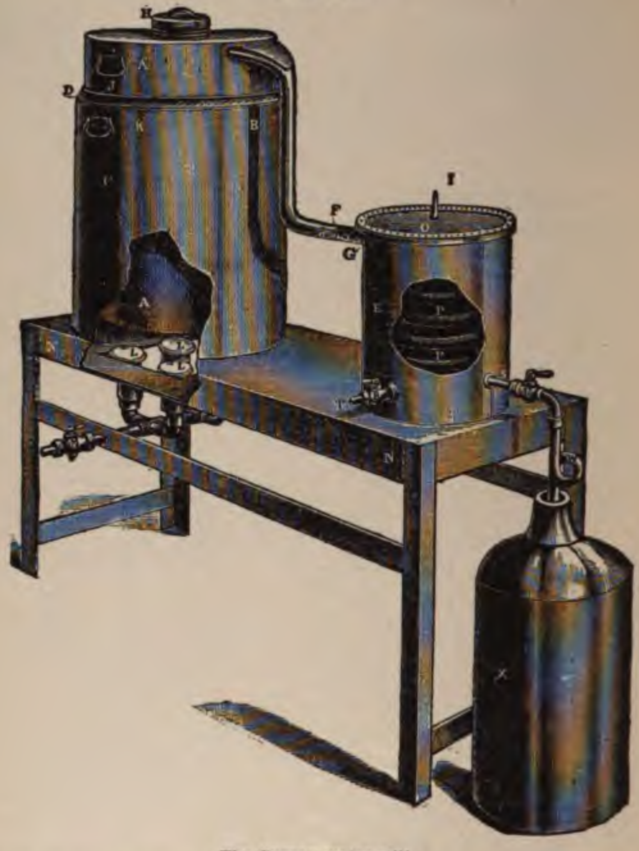
Aromatic waters made by distillation possess in many instances a more agreeable flavor than the aqueous solution of the corresponding volatile oils, which is probably due to the fact that, besides the volatile oil, other volatile compounds, such as acids or ethers, are present in the drug, and, passing over with the steam, remain dissolved in the condensed water. In distilling aromatic waters over a naked fire care should be taken to prevent the material from being scorched, which can be obviated by placing the drug either upon a diaphragm or in a perforated vessel or wire cage, and then suspending this in the water. A peculiar odor is observed in some waters immediately after they have been distilled and condensed in tin vessels, but not when glass vessels have been used; if the waters be exposed to the air in loosely stoppered vessels for a few days, this still-odor disappears and the natural odor of the water becomes apparent.

The *stronger* orange flower and rose waters are obtained, on a large scale, often as by-products in the distillation of the respective oils; in commerce they are distinguished as of *triple* or *quadruple* strength. In order to produce a saturated solution of the oil, recourse is had to the process of *cohobation* or redistillation, which consists in distilling the same water two or three times with fresh portions of the flowers. In some factories saturated orange flower and rose waters are obtained, not as by-products, but direct from the flowers, by distilling them with relatively small quantities of water; thus triple strength water is distilled by using 3 parts of the flowers to 1 of water, etc. According to Schimmel & Co., sextuple rose water represents the highest obtainable concentration, and rose water prepared from more than 6 times its weight of roses will not retain the whole of its oil in solution at ordinary temperature.

For the preparation of distilled water a special apparatus has been put upon the market, which is said, by those who have used it, to yield an exceptionally pure water and in considerably larger quantity than is usually expected from a still of like size. The apparatus, which is illustrated in Fig. 213, is known as the Curran water still, and can be used anywhere if gas and constant water-supply be available.

The tin-lined copper boiler has a capacity of 5 gallons, and from it $4\frac{1}{2}$ gallons of distilled water can be obtained in about two and a half hours; this allows the first quart of distillate, carrying with it all volatile matter, to be rejected, and also retains a quart of water in the boiler. The rapid vaporization of the water in the boiler is effected by means of four rose burners consuming jointly about 25 cubic feet of gas per hour, the generated heat being all utilized on the

FIG. 213.



The Curran water still.

A is a tin-lined copper boiler. C is a galvanized jacket for supporting the boiler over the gas-burners, and it is attachable at B, B; it is also intended to act as a flue to utilize the heat from the gas-burners on the sides of the boiler. H is a screw cover removable for filling or cleansing the boiler. F is the vapor-pipe from the boiler to the condensing coil, P, in the galvanized iron condensing tank, E, which is provided with an inlet for cold water at T, and an outlet for warm water at I. At G is a union for connecting the vapor-pipe with the condensing coil. S is the outlet for the condensed water, and X is the receiving vessel. J is a perforated ring resting on the jacket, and K are vent holes in the ring through which the exhausted gases pass off. O is a removable cover for cleansing the condensing tank. R is a faucet for drawing off the water from the condensing tank. L, L, L, are the gas-burners, and N the iron frame supporting the apparatus and burners. M is a gas cock for regulating the supply of gas to the burners.

bottom and sides of the boiler, which is surrounded by a galvanized iron jacket, as shown in the illustration. The vapor-pipes passing from the boiler, and the condensing coil, are both heavily lined with pure block tin, thus avoiding contact of the water with any other metal. There is no pressure on any part of the apparatus, the vapor being condensed as fast as generated and the distillate passing rapidly into the receiving vessel. Larger sizes of the Curran water still are made for use with gas or coal, delivering, according to the manufacturers' statements, which are guaranteed, from 4 to 10 gallons of distilled water per hour.

CHAPTER XIV.

THE OFFICIAL SOLUTIONS OR LIQUORS.

THE term Liquor as used in the U. S. Pharmacopœia is generally applied to aqueous solutions of non-volatile substances. The exceptions are Liquor Ammonii Acetatis, completely volatilized by boiling; Liquor Antisepticus, a hydro-alcoholic solution of volatile substances; Liquor Chlori Compositus, an aqueous solution of gaseous substances, containing also a small quantity of non-volatile matter; Liquor Formaldehydi, an aqueous solution of gaseous formaldehyde; Liquor Iodi Compositus, from which all the iodine can be volatilized by boiling, and much of it at even lower temperature. In Europe the term is indiscriminately applied to alcoholic, aqueous, and hydro-alcoholic solutions of non-volatile and volatile inorganic and organic matter. Twenty-five liquors are officially recognized, and of these 10 are made by simple solution of the medicinal agent in the solvent, while 15 involve chemical action in their preparation. The official liquors may therefore be conveniently divided into two groups, as follows:

1. **Simple Solutions.**—The active ingredient is added directly to the water.

Latin Name.	English Name.	Composition.
Liquor Acidi Arsenosi	Solution of Arsenous Acid . . .	Arsenic Trioxide, 10 Gm. Diluted Hydrochloric Acid, 50 Gm. Distilled Water, sufficient to make 1000 Gm.
Liquor Antisepticus .	Antiseptic Solution	Boric Acid, 20 Gm.; Benzoic Acid, 1 Gm.; Thymol, 1 Gm.; Eucalyptol, 0.25 Cc.; Oil of Peppermint, 0.50 Cc.; Oil of Gaultheria, 0.25 Cc.; Oil of Thyme, 0.10 Cc.; Alcohol, 250 Cc.; Water, sufficient to make 1000 Cc.
Liquor Arseni et Hydrargyri Iodidi . .	Solution of Arsenous and Mercuric Iodide (Donovan's Solution)	Arsenous Iodide, 10 Gm. Red Mercuric Iodide, 10 Gm. Distilled Water, sufficient to make 1000 Gm.
Liquor Calcis	Solution of Lime (Lime Water).	Saturated; contains about 0.17 per cent. of Calcium Hydroxide at 15° C. (59° F.), but the percentage decreases as the temperature rises.
Liquor Formaldehydi	Solution of Formaldehyde . .	An aqueous solution, containing not less than 37 per cent. by weight of absolute formaldehyde.
Liquor Iodi Compositus	Compound Solution of Iodine (Lugol's Solution)	Iodine, 5 Gm. Potassium Iodide, 10 Gm. Distilled Water, 85 Gm.

Latin Name.	English Name.	Composition.
Liquor Plumbi Subacetatis Dilutus . .	Diluted Solution of Lead Subacetate (Lead Water) .	Solution of Lead Subacetate, 40 Gm. Distilled Water, 960 Gm.
Liquor Potassii Hydroxidi	Solution of Potassium Hydroxide	Potassium Hydroxide (85 per cent. strength), 60 Gm. Distilled Water, 940 Gm.
Liquor Sodii Hydroxidi.	Solution of Sodium Hydroxide	Sodium Hydroxide (90 per cent. strength, 56 Gm. Distilled Water, 944 Gm.
Liquor Sodii Arsenatis	Solution of Sodium Arsenate .	Sodium Arsenate (anhydrous), 1 Gm. Distilled Water, sufficient to make 100 Gm.

2. Chemical Solutions.—The active ingredient is formed in the process of manufacture, as the result of chemical action.

Latin Name.	English Name.	Process of Manufacture.
Liquor Ammonii Acetatis	Solution of Ammonium Acetate (Spirit of Mindererus) . . .	Made by dissolving 5 Gm. of ammonium carbonate in 100 Cc. of diluted acetic acid. Contains about 7 per cent. of ammonium acetate.
Liquor Chlori Compositus	Compound Solution of Chlorine	Made by adding Hydrochloric Acid, 18 Cc., diluted with Water, 20 Cc., to Potassium Chlorate, granulated, 5 Gm. contained in a flask, heating for 2 or 3 minutes, and then adding two successive portions of 500 Cc. of distilled water. The solution, when freshly prepared, contains about 0.4 per cent. of chlorine, with some oxides of chlorine and potassium chloride.
Liquor Cresolis Compositus	Compound Solution of Cresol .	Made by incorporating Cresol, 500 Gm., with a mixture of Potassium Hydroxide, 80 Gm., dissolved in Water, 50 Cc., and Linseed Oil, 350 Gm. Finally, sufficient water is added to bring the total weight up to 1000 Gm.
Liquor Ferri Chloridi	Solution of Ferric Chloride . . .	Made from iron wire, hydrochloric acid, and water, with the aid of nitric acid. Contains not less than 29 per cent. of anhydrous ferric chloride.
Liquor Ferri et Ammonii Acetatis (Mistura Ferri et Ammonii Acetatis)	Solution of Iron and Ammonium Acetate (Basham's Mixture)	Made by mixing tincture of ferric chloride, solution of ammonium acetate, diluted acetic acid, aromatic elixir, glycerin, and water.
Liquor Ferri Subsulphate	Solution of Ferric Subsulphate (Monsel's Solution)	Made by adding ferrous sulphate to a heated mixture of nitric and sulphuric acids and water. Contains basic ferric sulphate corresponding to not less than 13.57 per cent. of metallic iron.
Liquor Ferri Tersulphatis	Solution of Ferric Sulphate . . .	Made like the preceding solution, except that a larger proportion of sulphuric acid is used. Contains about 36 per cent. of normal ferric sulphate.
Liquor Hydrargyri Nitratis	Solution of Mercuric Nitrate .	Made by dissolving red mercuric oxide in a mixture of nitric acid and water. Contains about 60 per cent. of mercuric nitrate.

Latin Name.	English Name.	Process of Manufacture.
Liquor Magnesii Citratis	Solution of Magnesium Citrate	Made by dissolving magnesium carbonate in a solution of citric acid; then adding syrup of citric acid and water, and finally potassium bicarbonate. Represents about 6.25 Gm. of magnesia in 360 Cc.
Liquor Plumbi Subacetatis	Solution of Lead Subacetate (Goulard's Extract)	Made by boiling lead oxide with a solution of lead acetate. Should contain not less than 25 per cent. of basic lead acetate.
Liquor Potassii Arsenitis	Solution of Potassium Arsenite (Fowler's Solution)	Made by dissolving arsenic trioxide and potassium bicarbonate in boiling water and adding compound tincture of lavender.
Liquor Potassii Citratis (Mistura Potassii, Citratis)	Solution of Potassium Citrate (Neutral Mixture)	Always freshly made by mixing a solution of potassium bicarbonate with one of citric acid, and containing not less than 8 per cent. of potassium citrate.
Liquor Sodæ Chlorinatæ	Solution of Chlorinated Soda (Labarraque's Solution)	Made by adding a hot solution of sodium carbonate to a solution of chlorinated lime. The chlorine compounds of sodium present should contain at least 2.4 per cent. of available chlorine.
Liquor Sodii Phosphatis Compositus	Compound Solution of Sodium Phosphate	Made by triturating sodium phosphate, 1000 Gm., sodium nitrate, 40 Gm., and citric acid, 130 Gm., together until completely liquefied and then adding sufficient distilled water to bring the volume up to 1000 Cc.
Liquor Zinci Chloridi	Solution of Zinc Chloride	Made by dissolving granulated zinc in hydrochloric acid and water, and freeing the solution from iron by means of nitric acid and zinc carbonate. Contains about 50 per cent. of zinc chloride.

CHAPTER XV.

DECOCTIONS AND INFUSIONS.

DECOCTIONS.

DECOCTIONS are aqueous solutions of the active principles of vegetable drugs, prepared at a boiling temperature. This process is obviously not adapted to drugs containing volatile principles, nor to those whose activity depends upon resinous constituents. Drugs of a very close texture, or the active virtues of which cannot be exhausted below the temperature of boiling water, are best suited for the process of decoction. In former years decoctions were extensively employed, and frequently made by using a large quantity of water and boiling it down, in open vessels, to one-half, or even to a less amount. This method offered no obvious advantage, and, in fact, often proved decidedly disadvantageous on account of the deleterious effect upon the constituents of the drug from long exposure to air and heat. In this country, at least, decoctions have almost entirely disappeared from the physician's armamentarium, and the pharmacist is but rarely called upon to prepare them.

Decoctions as well as infusions must always be prepared extemporaneously, since they will readily deteriorate on account of the perishable matter in solution and the absence of alcohol or other preservative.

The Pharmacopœia gives the following general directions for preparing decoctions whenever a special strength is not indicated by the physician: Put 50 Gm. of the substance, coarsely comminuted, into a suitable vessel provided with a cover; pour upon it 1000 Cc. of cold water, cover well, and boil for fifteen minutes; then let it cool to about 40° C. (104° F.), strain the liquid, and pass through the strainer enough cold water to make the product measure 1000 Cc.

The use of cold water, to begin with, insures the complete extraction from the drug of all its soluble principles, by the gradually heated water, the albuminous matter being subsequently coagulated as the heat is increased to near the boiling-point. If, on the other hand, the drug be at once immersed in boiling water, the albumen contained in cells would be coagulated, and thus seriously interfere with the extraction of the other constituents. In preparing compound decoctions, all the drugs may be added to the cold water, with the exception of those which, like senna, are injured by long-continued heat, or which contain aromatic or other volatile principles; such should be added when the decoction is ready to be removed from the fire or steam-bath, and allowed to digest until it is sufficiently cooled for straining. The material should in all cases be cut or bruised, the degree of fineness depending upon the nature of the tissue. Woody drugs may be reduced to a moderately fine powder; leaves, however, and other drugs consisting mainly of loose parenchyma, are better used in the form of a moderately coarse or very coarse powder.

Unless the liquid is to be considerably boiled down, decoctions are best prepared in a vessel provided with a cover, which may be loosely put on until the boiling is completed, when the vessel should be well closed, particularly if additions have been made at the close of boiling. Porcelain is undoubtedly the best material for vessels used for preparing decoctions, since it is not acted upon by the various vegetable principles; for similar reasons, glass flasks will answer a useful purpose in making small quantities of these preparations. As a rule, it is best to avoid metallic vessels, except when made of block tin and used in connection with a steam bath. As many drugs contain tannin, vessels made of iron are not adapted for preparing their decoctions, and the usually imperfect covering of galvanized or tinned sheet iron renders vessels lined with such material but little better suited for this purpose, and still inferior to properly enamelled iron vessels.

As a rule, decoctions should be allowed to cool below 40° C. (104° F.) before they are strained; principles which are soluble only in hot water are then mostly precipitated, and removed without, in most cases, weakening the medicinal value of the preparations; but, even with this precaution, the strained liquid may become unsightly in appearance through the further deposition, on cooling, of apotheme or matter soluble only in hot water. In such cases the pharmacist should be guided by the directions of the Pharmacopœia or the intentions of the physician, and not sacrifice effect to elegance.

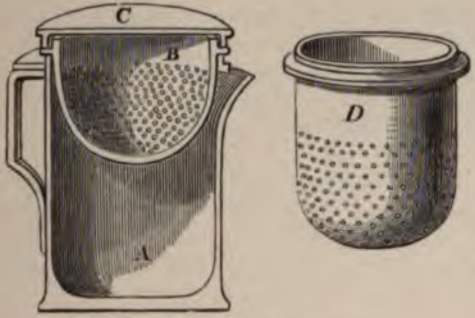
In the British Pharmacopœia, 13 decoctions are recognized, all of which are directed to be made with distilled water, and in the majority of the formulas boiling is directed to be continued for only ten minutes.

The German Pharmacopœia directs decoctions to be made of the strength of 10 per cent. when not otherwise specified, by adding the drug to cold water and keeping the mixture for half an hour in a bath of steam arising from boiling water, and then expressing while warm. Two preparations termed *decoctions*, of althæa and of flaxseed, are prepared cold by maceration for half an hour and subsequent gentle expression; they belong more properly under the head of *mucilages*.

INFUSIONS.

Infusions are aqueous solutions of the soluble principles of vegetable or animal drugs, obtained by maceration or digestion in hot or cold water, and differ from decoctions only in the lower degree of heat employed in their preparation. This process is particularly suitable for substances containing volatile or other principles which would be dissipated or injured by boiling. A convenient apparatus, well adapted for making these preparations, is Squire's infusion-pot, Fig. 214. This consists of the jar, A, with a projecting ledge near the top, which supports a strainer, B or D, containing the material to be exhausted; the jar is closed by a well-fitting cover, C. The advantages of this contrivance are that the material is exhausted by circulatory displacement—the liquid, as it becomes charged with the soluble ingredients, descending to the bottom, giving place to fresh portions of less saturated menstruum—and that no further straining will be required if care has been taken to use not too fine a powder.

Fig. 214.



Squire's infusion-pot.

Drugs are best adapted for exhaustion with water when cut into thin slices by means of a suitable knife, so that they may easily be permeated by the liquid; if cutting be inadmissible, they should be bruised to a coarse powder. Ligneous drugs, however, should be in a fine or moderately fine powder, which is best adapted also for most of those infusions which may be made by percolation.

Wherever possible, infusions should be made in porcelain or porcelain-lined vessels, to avoid contact with metal.

The U. S. Pharmacopœia has adopted the plan of ordering all infusions, unless otherwise directed by the physician, with the exception of four specially enumerated, to be made of 1 part of material to 20 parts of infusion, according to the following directions: "An ordinary infusion, the strength of which is not directed

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by the physician nor specified by the Pharmacopœia, shall be prepared by the following formula: Take of the substance, coarsely comminuted, 50 Gm.; boiling water, 1000 Cc.; water, a sufficient quantity to make 1000 Cc. Put the substance into a suitable vessel provided with a cover, pour upon it the boiling water, cover the vessel tightly, and let it stand for one-half hour in a warm place. Then strain, and pass sufficient water through the strainer to make the infusion measure 1000 Cc.

The Pharmacopœia omits to direct the expression of the drug after infusion, but it is evident that bulky herbs and flowers, which are best adapted to this process, would retain a considerable proportion of the liquid, which cannot be washed out simply by passing water through the strainer to make up the deficiency in volume.

Both in the cases of decoctions and infusions the Pharmacopœia requires that, when made of energetic or powerful substances, the physician shall specify the desired strength.

Three infusions are officially recognized in the Pharmacopœia—one prepared cold by percolation, and two by maceration with hot water; the time directed for the latter method is specified.

The strength of infusions of the German Pharmacopœia is double that of our own, but the general directions given for their preparation are nearly identical with the above, from which they differ only in that the mixture of drug and boiling water is heated for five minutes in a vapor-bath of boiling water, occasionally stirred, allowed to cool, and strained.

Official Infusions.

Made by Percolation.

Latin Name.	English Name.	Method of Preparation.
Infusum Pruni Virginianæ	Infusion of Wild Cherry	Macerate 40 Gm. of wild cherry in No. 20 powder with 60 Cc. of water for one hour, pack firmly in a percolator and slowly pass water through the drug, collecting the percolate in a bottle containing 50 Cc. of glycerin, until the total volume of infusion measures 1000 Cc.

If carefully made, infusion of wild-cherry bark is an efficient preparation, containing the hydrocyanic acid and volatile oil generated by prolonged contact with water. The glycerin improves the taste of the infusion somewhat, but is not sufficient to preserve the liquid for any length of time. Hot water should never be used for making this infusion, as it prevents the reaction desired between certain principles of the bark.

MADE BY HOT MACERATION.

Latin Name.	English Name.	Method of Preparation.
Infusum Digitalis . .	Infusion of Digitalis	Upon 15 Gm. of digitalis pour 500 Cc. of boiling water and let it macerate in a covered vessel for 1 hour. Then strain and to the liquid add 100 Cc. of alcohol and 150 Cc. of cinnamon water, and pass enough cold water through the residue to make the liquid measure 1000 Cc.
Infusum Sennæ Compositum	Compound Infusion of Senna (Black Draught)	Pour 800 Cc. of boiling water upon 60 Gm. of senna, 120 Gm. of manna, and 20 Gm. of bruised fennel and macerate in a covered vessel for half an hour. Express, and in the strained infusion dissolve 120 Gm. of magnesium sulphate. Again strain and pass enough cold water through the first residue to make the liquid measure 1000 Cc.

Infusion of digitalis is pleasantly flavored with cinnamon water, and contains 10 per cent. by volume of alcohol; hence it will keep for a day or two, particularly in a cool place. It should be made fresh whenever prescribed, unless in frequent demand, as in hospitals, when daily fresh preparation may suffice.

CHAPTER XVI.

SYRUPS.

In pharmacy the term syrup is applied to concentrated solutions of sugar, the solvent being either water or an aqueous, acetous, or hydro-alcoholic solution of some medicinal or aromatic principle. The Pharmacopœia applies the name *syrupus* or *syrup* to a nearly saturated solution of sugar in water; in practice this solution is usually termed *simple syrup* as a mark of distinction. Syrups are an old and favorite form of administering medicines, partly on account of the sweet taste, and partly because sugar is used as a preservative for otherwise unstable vegetable solutions, in place of alcohol, which is often contraindicated in disease. The sugar used in making syrups should be of the best quality obtainable, as upon it depend the character and stability of the finished syrup. The Pharmacopœia describes sugar as occurring in white, hard, crystalline granules, of purely sweet taste, which corresponds to the best commercial varieties known as granulated and cut-loaf sugar; in order to overcome the yellowish cast of sugar, refiners frequently add ultramarine, Prussian blue, etc., which will pass to some extent even through paper filters and finally deposit in the syrup containers.

Sugar is soluble in half its weight of water at 15° C. (59° F.), and a saturated solution thus prepared has the specific gravity of 1.345; it is also soluble in 175 times its weight of official alcohol. Large quantities of sugar dissolved in water very materially increase the bulk of the liquid, a fact which must always be borne in mind in the preparation of syrups; practically, two-thirds of the weight of sugar will equal its bulk in fluid measure, or, in other words, 750 Gm. of sugar when dissolved in water will increase the bulk of the liquid by nearly 500 Cc. The proper proportion of sugar to menstruum is of great importance, as upon it depends the stability of the syrup. Should the sugar be deficient in quantity, it will not efficiently protect the other organic principles in the syrup, and the latter would be liable to ferment. On the other hand, if too much sugar be dissolved by the aid of heat, the excess will crystallize after cooling and dispose an additional quantity to separate in like manner, thus leaving the syrup weaker in sugar than it should be and subject to similar alterations as if an insufficient quantity of sugar had been used. If alcohol be present in the menstruum, less sugar will be taken up by the liquid than in the case of pure water as shown by the following table, but at the same time less sugar is required to insure stability owing to the preservative properties of the alcohol.

SOLUBILITY OF CANE-SUGAR IN MIXTURES OF ALCOHOL AND WATER.

(According to Schufeldt.)

Percentage of Alcohol in the Mixture.		Percentage of Sugar in Solution.	Number of Grammes of Sugar soluble in 100 Cc. of the Mixture.
By Volume.	By Weight.		
0.	0.	66.20	195.8
6.	5	64.25	179.7
12.	10	62.20	164.5
18.	15	60.40	152.5
24.	20	58.55	141.2
30.	25	56.20	128.3
36.	30	54.05	117.8
42.	35	51.25	105.3
47.	40	47.75	91.3
58.5	50	38.55	62.7
67.5	60	26.70	36.4
77.	70	12.25	13.9
85.5	80	4.05	4.2
93·5	90	0.95	0.09
96.75	95	0.15	0.01

Preparation.—In the preparation of syrups, solution of the sugar may be effected by one of the following methods: Agitation of sugar and solvent without heat, cold percolation of the sugar with the solvent, gentle heating of the sugar and solvent, or heating the mixture of sugar and solvent to the boiling-point. The application of heat in the manufacture of syrups should be avoided as far as possible, especially a boiling temperature, partly to prevent the loss of volatile constituents and partly to guard against any change in the character of the sugar, which, under the influence of heat and particularly with acid liquids, is converted into inverted sugar, resembling glucose, and thereby predisposed to fermentation; moreover, the use of heat in open vessels causes evaporation of a part of the solvent, which, if not restored, produces a supersaturated solution with the attending evil of crystallization referred to above.

The preparation of syrups without heat is a feature of American pharmacy, both the British and German Pharmacopœias directing the use of heat in every instance. By some authorities it is claimed that syrups made with heat are more permanent than those made cold; this claim is not supported by experience in this country. For all syrups containing volatile principles or such as may be changed by heat, the cold process is decidedly preferable, and if pure sugar be used, such syrups keep admirably.

The process of cold percolation of sugar with the solvent was first suggested by L. Orinsky in 1871, and is now largely recommended in the Pharmacopœia; the process is of decided advantage whenever the syrup is to be prepared without heat, although it requires a little care in its management so as to insure perfect solution and a clear percolate. A cylindrical, slightly tapering percolator is best adapted for the purpose. A clean, soft piece of sponge is placed, with moderate pressure, in the neck of the percolator (if too tightly compressed, the viscid liquid will not pass through; and if too loose, the liquid passes too rapidly and not clear); upon it is poured the sugar in granular form, and properly levelled and shaken down by tapping the sides of the percolator, after which a diaphragm of filter paper is laid on the surface and the solvent carefully poured on with the aid of a guiding rod. If the sponge or a tuft of absorbent cotton has been properly adjusted, the solution will be perfectly clear and transparent, and pass out in drops only, all the sugar being taken up before the end of the process; but if the liquid passes too rapidly, or if it be turbid, it must be poured back into the percolator until the defect is remedied. It will be found advantageous to close the lower orifice of the percolator with a sound cork (or if a rubber tube be used, to tie the same up on the side of the percolator) as soon as the menstruum reaches the sponge or cotton, and allow it to remain closed for a short while, possibly an hour or two, so that the menstruum may have an opportunity of becoming saturated, and thus a more gradual and more satisfactory flow of the percolate be established. Some objections have been made to this process, such as the time necessary for perfect solution of the sugar, and the fact that albuminous principles liable to induce fermentation are best removed by heat; but it must be borne in mind that cold percolation requires very little attention after it has once been started, can be allowed to go on during the night, and does away with the necessity of subsequent filtration; the evil tendency of nitrogenized principles in the solvent may be overcome by the use of weak alcohol and glycerin, as is directed in many of the official formulas.

In the case of some syrups, where the viscid character of the solvent precludes rapid solution of the sugar, or when the syrup is wanted in a hurry, a moderate heat may be employed to facilitate solution, by putting the sugar and solvent into a strong bottle one and a half times as large as the required volume of syrup, and, after securely corking, keeping it in a water-bath at a temperature of about 50° C. (122° F.), and frequently agitating until perfect solution is effected; all loss of volatile principles is avoided by keeping the bottle well corked. Whenever the solvent contains latent ferments or a large proportion of albuminous matter, heating to the boiling-point is necessary, in order to render such principles harmless, as in the case of syrups prepared from fruit juices; but the heat should not be continued beyond the boiling-point, to avoid a change in the sugar.

When large quantities of syrup are to be made with heat, the mixture of sugar and solvent is placed in a porcelain-lined or well-tinned kettle and heated over a direct fire or on a steam-bath until the sugar is dissolved; it is then strained and water added to make up the desired volume.

Fruit syrups are no longer recognized in the U. S. Pharmacopœia. They are usually prepared by crushing the fruit and setting it aside at a moderate temperature, 20° to 25° C. (68°–77° F.), for several days, for the purpose of destroying certain undesirable principles known as pectin or vegetable jelly, which, if allowed to remain in the fruit juice, are apt to cause the syrup to gelatinize. The complete removal of pectin is determined by means of alcohol, which should mix clear with twice its volume of the fruit juice; a concentrated solution of magnesium sulphate should also leave the filtered juice unaffected.

The fermentation of fruit juices is usually conducted in casks or containers tightly closed, but provided with a suitable means of escape for the carbon dioxide gas generated during the process, which latter is allowed to pass by means of a glass tube through water contained in a small bottle; the end of the fermentative process is indicated when gas-bubbles cease to escape through the water. Experience has shown that the addition of a small quantity of sugar (2 per cent. of the weight of the fruit) hastens fermentation, preserves the color, and facilitates subsequent filtration of the juice.

After removal of the pectin the pulp is expressed and the juice allowed to subside in well-closed vessels, in a cool place, for two or three days until clear; the supernatant liquid must be carefully decanted or withdrawn and passed through a previously wetted paper filter. Sugar to the extent of 6 pounds to every 4 pounds of filtered juice should be added to the filtrate without delay and dissolved by stirring before the mixture is heated to boiling; any albuminous matter remaining in the juice is coagulated by heating and removed by subsequent straining. The mixture of filtered juice and sugar must not be boiled for any length of time, but the heat should be withdrawn when the syrup begins to boil quietly after the first frothing and rising of the liquid.

This process is applicable alike to the syrups of blackberries, cherries, raspberries, and strawberries.

Preservation.—Syrups are best preserved in completely filled bottles, in a cool place, and will keep unaltered for a long time if properly prepared; the addition of preservatives, such as salicylic or boric acid, calcium sulphite, ether, etc., is unnecessary, and, in fact, objectionable, and such syrups as cannot be kept with ordinary care should be made in small quantity only. It is well known that syrups containing acids gradually show a change in the sugar from cane-sugar to inverted sugar, and it has been shown in an interesting series of experiments with the official syrups, by Woltersdorf and Richtmann, 1900, that the inversion is in direct proportion to the temperature to which the syrup is exposed; also that mineral acids cause greater inversion than organic acids, and that the presence of neutral salts in the syrup has the tendency to retard the inverting action of the acid. Air and heat are far more detrimental to the stability of sugar solutions than diffused light; but direct sunlight should always be avoided on account of the heat transmitted by the sun's rays. When syrups have undergone fermentation they are no longer fit for use, and even if the attempt be made to restore them by boiling, they are likely soon to spoil again, owing to the decreased proportion of sugar left in solution; the best and safest plan is to throw them away. Finished syrups should always be put into perfectly *clean and dry* bottles (if made by heat, not until they have become cold), so as to avoid dilution and possible contamination with fermentation germs, which are likely to lurk in imperfectly cleaned bottles. Bottles from which syrups have been dispensed should be thoroughly washed with weak lye and afterward with water, and then dried before they are refilled.

All syrups, whether made by cold or hot process (except cold percolation), require straining through flannel previously moistened and expressed to remove particles of dust and dirt; and in the case of colorless or light-colored syrups, their appearance will be greatly improved by filtering them, under cover, through paper or a pledget of cotton.

ALPHABETICAL LIST OF OFFICIAL SYRUPS.

Latin Name.	English Name.	Proportion of Ingredients.
Syrupus	Syrup	Sugar, 850 Gm.; Distilled Water sufficient to make 1000 Cc.
Syrupus Acaciæ . . .	Syrup of Acacia .	Acacia, selected, 100 Gm.; Sugar, 800 Gm.; Distilled Water, 430 Cc., or sufficient to make 1000 Cc.
Syrupus Acidi Citrici	Syrup of Citric Acid	Citric Acid, 10 Gm.; Water, 10 Cc.; Tincture of Fresh Lemon Peel, 10 Cc.; Syrup sufficient to make 1000 Cc.
Syrupus Acidi Hydriodici	Syrup of Hydriodic Acid . .	Absolute Hydriodic Acid, 1 per cent., held in solution in Syrup, and preserved by the presence of a small proportion of hypophosphorous acid.
Syrupus Amygdalæ .	Syrup of Almond	Spirit of Bitter Almond, 10 Cc.; Orange Flower Water, 100 Cc.; Syrup sufficient to make 1000 Cc.
Syrupus Aurantii . .	Syrup of Orange	Tincture of Fresh Orange Peel, 50 Cc.; Citric Acid, 5 Gm.; Sugar, 820 Gm.; Water sufficient to make 1000 Cc.
Syrupus Aurantii Florum	Syrup of Orange Flowers . . .	Sugar 850 Gm.; Orange Flower Water sufficient to make 1000 Cc.
Syrupus Calcii Lactophosphatis	Syrup of Calcium Lactophosphate	To a solution of Calcium Lactophosphate prepared from Calcium Carbonate, 25 Gm.; Lactic Acid, 60 Cc.; Phosphoric Acid, 36 Cc.; and Water, 300 Cc., are added Orange Flower Water, 50 Cc.; Sugar, 725 Gm., and Water sufficient to make 1000 Cc.
Syrupus Calcis . . .	Syrup of Lime .	Lime, 65 Gm.; Sugar, 350 Gm.; Water sufficient to make 1000 Cc.

Latin Name.	English Name.	Proportion of Ingredients.
Syrupus Ferri Iodidi	Syrup of Ferrous Iodide	Ferrous Iodide, 5 per cent., held in solution in syrup. The ferrous iodide is obtained by allowing iodine, 41.5 Gm., to react on iron wire, 12.5 Gm., in the presence of distilled water, 150 Cc. When reaction has ceased, the mixture is heated to boiling and sugar, 50 Gm., dissolved therein. The solution is then filtered into sugar, 550 Gm., the filter washed with distilled water, 125 Cc., which is also added to the sugar, and the latter then dissolved by heat. After perfect solution the liquid is strained, diluted hypophosphorous acid, 20 Cc., and sufficient distilled water added to bring the weight of the finished product up to 1000 Gm.
Syrupus Ferri, Quininæ et Strychninæ Phosphatum	Syrup of the Phosphates of Iron, Quinine, and Strychnine	Glycerite of the Phosphates of Iron, Quinine, and Strychnine, 1 volume; Syrup, 3 volumes.
Syrupus Hypophosphitum	Syrup of Hypophosphites	Calcium Hypophosphite, 45 Gm.; Potassium and Sodium Hypophosphites, of each 15 Gm.; Diluted Hypophosphorous Acid, 2 Gm.; Sugar, 650 Gm.; Tincture of Fresh Lemon Peel, 5 Cc.; Water sufficient to make 1000 Cc.
Syrupus Hypophosphitum Compositus	Compound Syrup of Hypophosphites	Calcium Hypophosphite, 35 Gm.; Potassium and Sodium Hypophosphites, of each 17.5 Gm.; Ferric and Manganese Hypophosphites, of each 2.25 Gm.; Quinine, 1.1 Gm.; Strychnine, 0.115 Gm.; Sodium Citrate, 3.75 Gm.; Diluted Hypophosphorous Acid, 15 Cc.; Sugar, 775 Gm.; Water sufficient to make 1000 Cc.
Syrupus Ipecacuanhæ	Syrup of Ipecac	Fluidextract of Ipecac, 70 Cc.; Acetic Acid, 10 Cc.; Glycerin, 100 Cc.; Sugar, 700 Gm.; Water sufficient to make 1000 Cc.
Syrupus Krameriæ	Syrup of Krameria	Fluidextract of Krameria, 450 Cc.; Syrup, 550 Cc.
Syrupus Lactucarii	Syrup of Lactucarium	Tincture of Lactucarium, 100 Cc.; Glycerin, 200 Cc.; Citric Acid, 1 Gm.; Orange Flower Water, 50 Cc.; Syrup sufficient to make 1000 Cc.
Syrupus Picis Liquidæ	Syrup of Tar	Tar, 5 Gm.; Alcohol, 50 Cc.; Sugar, 850 Gm.; Water sufficient to make 1000 Cc. The tar is first mixed with twice its weight of clean white sand and then washed with 100 Cc. of cold water; the residue is dissolved in the alcohol, triturated with magnesium carbonate, 10 Gm., and sugar, 50 Gm., and mixed with water, 400 Cc. After macerating for 2 hours the mixture is filtered and the remainder of the sugar dissolved in the clear filtrate, sufficient water being added to make 1000 Cc.

Latin Name.	English Name.	Proportion of Ingredients.
Syrupus Pruni Virginianæ	Syrup of Wild Cherry	Wild Cherry, 150 Gm.; Sugar, 700 Gm. Glycerin, 150 Cc.; Water sufficient to make 1000 Cc.
Syrupus Rhei	Syrup of Rhubarb	Fluidextract of Rhubarb, 100 Cc.; Spirit of Cinnamon, 4 Cc.; Potassium Carbonate, 10 Gm.; Water, 50 Cc.; Syrup sufficient to make 1000 Cc.
Syrupus Rhei Aromaticus	Syrup of Rhubarb (Aromatic)	Aromatic Tincture of Rhubarb, 150 Cc.; Potassium Carbonate, 1 Gm.; Syrup, 850 Cc.
Syrupus Rosæ	Syrup of Rose	Fluidextract of Rose, 125 Cc.; Diluted Sulphuric Acid, 10 Cc.; Sugar, 750 Gm.; Water sufficient to make 1000 Cc.
Syrupus Rubi	Syrup of Rubus	Fluidextract of Rubus, 250 Cc.; Syrup, 750 Cc.
Syrupus Sarsaparillæ Compositus	Syrup of Sarsaparilla (Compound)	Fluidextract of Sarsaparilla, 200 Cc.; Fluidextract of Glycyrrhiza, 15 Cc.; Fluidextract of Senna, 15 Cc.; Sugar, 650 Gm.; Oil of Anise, Oil of Gaultheria, and Oil of Sassafras, of each 0.2 Cc.; Water sufficient to make 1000 Cc.
Syrupus Scillæ	Syrup of Squill	Vinegar of Squill, 450 Cc ; Sugar, 800 Gm.; Water sufficient to make 1000 Cc.
Syrupus Scillæ Compositus	Syrup of Squill (Compound)	Fluidextract of Squill, 80 Cc.; Fluidextract of Senega, 80 Cc.; Antimony and Potassium Tartrate, 2 Gm.; Sugar, 750 Gm.; Water sufficient to make 1000 Cc.
Syrupus Senegæ	Syrup of Senega	Fluidextract of Senega, 200 Cc.; Syrup, 800 Cc.
Syrupus Sennæ	Syrup of Senna	Fluidextract of Senna, 250 Cc.; Oil of Coriander, 5 Cc.; Syrup sufficient to make 1000 Cc.
Syrupus Tolutanus	Syrup of Tolu	Tincture of Tolu, 50 Cc.; Sugar, 820 Gm.; Water sufficient to make 1000 Cc. After mixing the tincture with magnesium carbonate, 10 Gm., and sugar, 60 Gm., water, 450 Cc., are added with constant trituration and the mixture filtered. The remainder of the sugar is dissolved in the filtrate with the aid of a gentle heat, the solution strained, and sufficient water added to bring the volume to 1000 Cc.
Syrupus Zingiberis	Syrup of Ginger	Fluidextract of Ginger, 30 Cc.; Alcohol, 20 Cc.; Sugar, 820 Gm.; Water sufficient to make 1000 Cc. After mixing the fluidextract and alcohol with magnesium carbonate, 10 Gm., and sugar, 60 Gm., water, 450 Cc., are added with constant trituration and the mixture filtered. The remainder of the sugar is dissolved in the filtrate with the aid of a gentle heat, the solution strained, and sufficient water added to bring the volume up to 1000 Cc.

The official syrups may be conveniently divided into two classes, namely, those possessing little or no medicinal properties and chiefly used for flavoring purposes, and those used as therapeutic agents and conveniently termed medicated syrups.

To the first class, or flavoring syrups, belong the following:

Syrup, Syrup of Almond, Syrup of Citric Acid, Syrup of Ginger, Syrup of Orange, Syrup of Orange Flowers, and Syrup of Tolu.

The class of medicated syrups embraces the remaining official syrups, namely:

Syrup of Acacia, Syrup of Calcium Lactophosphate, Syrup of Ferrous Iodide, Syrup of Hydriodic Acid, Syrup of Hypophosphites, Syrup of Hypophosphites (Compound), Syrup of Ipecac, Syrup of Krameria, Syrup of Lactucarium, Syrup of Lime, Syrup of the Phosphates of Iron, Quinine, and Strychnine, Syrup of Rhubarb, Syrup of Rhubarb (Aromatic), Syrup of Rose, Syrup of Rubus, Syrup of Sarsaparilla (Compound), Syrup of Senega, Syrup of Senna, Syrup of Squill, Syrup of Squill (Compound), Syrup of Tar, and Syrup of Wild Cherry.

Of the 29 syrups recognized in the U. S. Pharmacopœia, 20 are directed to be made without heat, and of these, 7 are simple mixtures of syrup with the respective medicating fluids. Two of the remaining syrups are prepared by raising the ingredients to the boiling temperature; in 3 the sugar is dissolved with the aid of a gentle heat; and in the case of 4, solution of the sugar is effected by means of water-bath heat, temperature not specified, but necessarily below boiling.

TABLE SHOWING THE METHODS DIRECTED FOR THE OFFICIAL SYRUPS.

Cold Process.

Syrup of Almond.
" Calcium Lactophosphate.
" Citric Acid.
" Hydriodic Acid.
" Hypophosphites.
" Hypophosphites (Compound).
" Ipecac.
" Krameria.
" Lactucarium.
" Orange.
" Orange Flowers.
" Phosphates of Iron, Quinine, and Strychnine.
" Rhubarb.
" Rhubarb (Aromatic).
" Rose.
" Rubus.
" Senega.
" Senna.
" Squill (Compound).
" Wild Cherry.

Hot Process.

a. **Gentle Heat.**

Syrup of Sarsaparilla (Compound).
" Squill.
" Tar.

b. **Water-bath Heat.**

Syrup of Acacia.
" Ferrous Iodide.
" Ginger.
" Tolu.

c. **Boiling Temperature.**

Syrup.
Syrup of Lime.

SPECIAL REMARKS.

Syrupus.—Official simple syrup contains 64.54 per cent. by weight of sugar, each Cc. representing 0.85 Gm.; it should be made with distilled water, so as to produce a solution of crystalline clearness, and if heat be employed, the syrup should be passed through a small dry strainer, which is then washed with sufficient distilled water used for rinsing the vessel to bring the volume up to the required quantity. Simple syrup should be made and preserved with care. One pound measures very nearly 12 fluidounces.

Syrupus Acaciæ.—Syrup of acacia or syrup of gum arabic is prone to spoil, especially in warm weather, and should be preserved in small bottles in a cold place. Solution of the acacia will be materially facilitated if the distilled water be heated before the gum is added and the mixture then frequently stirred. If small quantities of the syrup are to be made extemporaneously, 3 Gm. (or 50 grains) of clean granulated acacia may be triturated with 6 Cc. (or 1½ fluidrachms) of distilled water until dissolved, and then mixed with sufficient syrup to produce 30 Cc. (or 1 fluidounce) of finished product.

Syrupus Acidi Citrici.—Syrup of citric acid, made by mixing tincture of fresh lemon peel and a solution of citric acid with simple syrup, is an excellent substitute for lemon syrup, being more stable and of uniform acidity. It is of pleasant flavor and slightly opalescent, each Cc. containing 0.010 Gm. of citric acid. Unfortunately syrup of citric acid, when kept on hand for some time, acquires a terebinthinate odor; it should therefore be made in small quantities.

Syrupus Acidi Hydriodici.—Syrup of hydriodic acid is intended by the present official formula to be made extemporaneously, with the view of avoiding discoloration. If the acid liquid is kept in contact with the syrup for some length of time, especially in warm weather, caramelization of the sugar will take place and the syrup becomes colored, growing gradually darker. Syrup of hydriodic acid having more than a pale-straw color should not be dispensed. In order to insure the exact strength of the syrup, 1 per cent. of absolute hydriodic acid, it should always be made by weight, using 1 part of diluted hydriodic acid, 3 parts of distilled water, and 6 parts of syrup. As the specific gravity of the official syrup of hydriodic acid is given as 1.190, each fluidounce will weigh 542.283 grains, or 4 fluidounces will weigh 2170 grains, corresponding to practically 140 Gm.

Syrupus Amygdalæ.—Syrup of almond of the present Pharmacopœia is entirely different from that heretofore officially recognized. It is a colorless liquid, having a pleasant mixed flavor of oil of bitter almond and orange flowers, and mixes clear with water. The former syrup of almond was made from almonds direct, and formed a milk-like liquid when mixed with water; it is known in Europe as *syrupus* *emulsivus.* When prescribed under the latter name, the present official syrup of almond should not be dispensed.

Syrupus Aurantii.—Syrup of orange is made from tincture of fresh orange peel by triturating the same with magnesium carbonate and water, and filtering the milky mixture; the filter is washed with more water until a definite volume of clear filtrate is obtained, in which the citric acid and sugar are dissolved by agitation. The finished syrup has a pleasant aroma and an acidulous taste, and mixes clear with aqueous liquids. Syrup of orange should never be made from fluidextract of sweet orange peel, as the latter is prepared from dried peel with a hydro-alcoholic menstruum, is without the fine orange flavor, and is more or less bitter; moreover, syrup of orange thus made turns liquids containing iron preparations dark, on account of the tannin in the fluidextract, which is not the case with the official syrup.

Syrupus Aurantii Florum.—Syrup of orange flowers contains the same proportion of sugar as simple syrup; it is made without the aid of heat, most conveniently by percolation.

Syrupus Calcii Lactophosphatis.—Syrup of calcium lactophosphate, sometimes erroneously called syrup of lactophosphate of lime, is easily prepared according to the official directions. The calcium carbonate should be added very gradually to the diluted lactic acid so that a perfect solution may result. When the phosphoric acid is to be added this should be diluted with more water than officially directed (at least twice as much water as acid should be used), and this mixture must be added slowly to the solution of calcium lactate previously prepared, constantly stirring with a glass rod, so as to avoid precipitation of calcium phosphate. The newly formed salt will be kept in solution by the excess of phosphoric acid and the lactic acid present, or will be dissolved almost immediately after it has been precipitated. The acid solution, after addition of more water, is filtered, and to the filtrate the orange-flower water and sugar are added, and the whole shaken until perfect solution has been effected. Like all syrups containing acid, this syrup is apt to become discolored if kept on hand for a long time. Each Cc. of the finished syrup represents 0.02584 Gm. of tricalcium phosphate.

Syrupus Calcis.—Advantage is taken, in the preparation of syrup of lime, of the well-known fact that sugar largely increases the solubility of lime in water, and this solubility varies with the proportion of sugar to the water used; according to Peligot, 100 parts of sugar contained in 250 parts of aqueous solution will take up 26.5 parts of lime, while the same quantity of sugar in 2000 parts of solution takes up only 18 parts of lime. Choice lime should be used—as free from carbonate and other impurities as possible. The official syrup of lime is of uncertain strength, the Pharmacopœia not having fixed a definite proportion, but when freshly made it contains probably 0.032 Gm. of calcium oxide in every Cc. The direction to boil the lime, sugar, and water together for five minutes is not essential, except to gain time, for cold maceration with frequent agitation will cause an equally large amount of lime to be dissolved; but longer time is necessary—possibly two or three days. Syrup of lime changes very rapidly upon exposure to air, and should, therefore, be kept in well-stoppered bottles.

Syrupus Ferri Iodidi.—The first step in making syrup of ferrous iodide is the preparation of a solution of iodide of iron, and care should be taken that no iodine is lost and that a pale-green solution free from all iodine odor be obtained. This is then protected by addition of sugar and filtered into the remainder of the sugar, the flask and filter being rinsed with an additional quantity of distilled water. The sugar is dissolved by heating on a water-bath and the syrup then strained, the diluted hypophosphorous acid added, and finally sufficient distilled water to bring the weight up to the required quantity. The hypophosphorous acid, being a valuable reducing agent, is added to prevent oxidation and consequent discoloration of the syrup, and has been found superior to other agents. The present official syrup of ferrous iodide is of only one-half the strength of former syrups, containing but 5 per cent. of ferrous iodide. This change was made so as to have the strength correspond to that of the syrup of other pharmacopœias.

Syrupus Ferri, Quininæ et Strychninæ Phosphatum (Syrup of the Phosphates of Iron, Quinine, and Strychnine, also known as Easton's Syrup).—The official formula directing the mixture of 1 volume of the glycerite of the phosphates of iron, quinine, and strychnine with 3 volumes of syrup is intended for extemporaneous preparation, as it is impossible to prevent discoloration and darkening of the syrup if the same be kept on hand for some time, owing to the action of the acid on the sugar. As now made, the syrup is almost colorless, slightly fluorescent, and has an intensely bitter taste. Each Cc. of the finished syrup contains 0.02 Gm. of soluble ferric phosphate, 0.026 Gm. of quinine, and 0.0002 Gm. of strychnine, the two latter also in the form of phosphates.

Syrupus Hypophosphitum (Syrup of Hypophosphites).—By this name the Pharmacopœia recognizes a syrup of the hypophosphites of calcium, potassium, and sodium, flavored with tincture of fresh lemon peel; it is prepared by making a solution of the three salts in water, acidulating the same with hypophosphorous acid, and in it dissolving the sugar by agitation. Each Cc. of the syrup contains 0.045 Gm. of calcium hypophosphite, 0.015 Gm. each of potassium and sodium hypophosphites, and 0.002 Gm. of dilute hypophosphorous acid.

Syrupus Hypophosphitum Compositus.—Compound syrup of hypophosphites differs from the preceding syrup in containing also the hypophosphites of iron, manganese, quinine, and strychnine, and in not being flavored with tincture of fresh lemon peel. The sodium citrate used is necessary to effect the solution of the ferric hypophosphite, forming a yellowish-green liquid. The quinine and strychnine are converted into hypophosphites by solution in the diluted hypophosphorous acid. The finished syrup has a greenish-yellow color and keeps well. Each Cc. contains 0.035 Gm. of calcium hypophosphite, 0.0175 Gm. each of potassium and sodium hypophosphite, 0.00225 Gm. each of ferric and manganese hypophosphite, 0.0011 Gm. of quinine (as hypophosphite) and 0.00015 Gm. of strychnine (as hypophosphite).

Syrupus Ipecacuanhæ.—Syrup of ipecac is made from the fluidextract of the drug, which is well shaken with a mixture of acetic acid and water, for the purpose of bringing the active principle into aqueous solution, and of rejecting those undesirable constituents which are apt to cause flocculi in the syrup; after filtration glycerin is added to the clear liquid, and then the sugar, after which the mixture is well shaken until perfect solution results. Formerly syrup of ipecac was likely to sour in warm weather, but this difficulty is now obviated by the presence of 10 per cent. of glycerin; each Cc. represents 0.070 Gm. of ipecac.

Syrupus Krameriæ.—Syrup of krameria, also known as syrup of rhatany, is prepared by mixing fluidextract of krameria with simple syrup, in the proportion of 45 volumes of the former to 55 volumes of the latter; each Cc. represents 0.45 Gm. of krameria.

Syrupus Lactucarii.—The present official formula for syrup of lactucarium is much simpler than that formerly given. The character of the finished syrup will depend upon that of the tincture of lactucarium used; if the latter has been carefully made so as to be free from the caoutchouc-like constituent of the drug, the resulting syrup should be clear and of a light-brownish color. Each Cc. of the syrup represents the active virtues of 0.05 Gm. of lactucarium.

Syrupus Picis Liquidæ (Syrup of Tar).—Tar always contains certain impurities which are readily soluble in cold water, and these it is intended to remove in the process officially directed for the syrup. Sand is mixed with the tar, before the addition of cold water, in order to facilitate the washing. The subsequent treatment with alcohol and water dissolves the active virtues of the tar, and a clear filtrate is obtained with the aid of magnesium carbonate, in which the sugar is then dissolved with the aid of a gentle heat. The finished product has a brownish-yellow color and a decided odor of tar. Each Cc. represents 0.05 Gm. of tar.

Syrupus Pruni Virginianæ (Syrup of Wild Cherry).—The preliminary maceration of the wild cherry with water for 24 hours causes a peculiar reaction or fermentation to take place between certain constituents of the bark, resulting in the formation of hydrocyanic acid and a volatile oil, which are extracted by subsequent percolation with water, until 3 Cc. of percolate have been collected for every Gm. of drug used, and in the percolate the sugar is dissolved without heat. Enough menstruum should be added to the powdered drug to moisten it thoroughly, and the percolator kept tightly closed to prevent loss of the hydrocyanic acid; a No. 20

powder being rather coarse, the mixture must be very firmly packed, so that the drug may be slowly exhausted. The present syrup is lighter in color than that of the 1890 Pharmacopœia and has a less astringent taste, owing to the fact that the glycerin is added to the aqueous percolate and is not allowed to act on the bark itself. The presence of 15 per cent. of glycerin aids in the preservation of the syrup. The amount of hydrocyanic acid present in the syrup is a very uncertain quantity, nor does it remain constant, owing to exposure and its volatile and unstable character.

Syrupus Rhei.—The official formula for syrup of rhubarb directs a solution of potassium carbonate to be added to fluidextract of rhubarb prior to its admixture with simple syrup; a small quantity of spirit of cinnamon is also added as a flavoring agent. The addition of an alkali prevents the separation of resinous matter by retaining the same in solution, and thus a clear syrup is obtained. The use of water for solution of the potassium carbonate appears quite unnecessary, since the alkali can be dissolved in a part of the simple syrup, and syrup of rhubarb thus prepared keeps admirably well. Each Cc. represents 0.100 Gm. of rhubarb.

Syrupus Rhei Aromaticus (Aromatic or Spiced Syrup of Rhubarb).—The object of adding potassium carbonate, which is readily soluble in the aromatic tincture of rhubarb, is to prevent precipitation of resinous matter, and thus produce a clear syrup.

Syrupus Rosæ.—The present official syrup of rose differs from those of former pharmacopœias in containing 1 per cent. by volume of diluted sulphuric acid, which imparts an agreeable acidulous taste to the finished syrup, and causes the color to be somewhat lighter.

Syrupus Rubi.—The official syrup of rubus, also known as syrup of blackberry root, is made by mixing 1 volume of fluidextract of blackberry bark with 3 volumes of syrup. It has a strongly astringent taste, and is of a deep reddish-brown color.

Syrupus Sarsaparillæ Compositus.—In the preparation of compound syrup of sarsaparilla a mixture is first made of the fluidextracts of sarsaparilla, senna, and glycyrrhiza, together with the oils of sassafras, anise, and gaultheria; this mixture, after the addition of about 370 Cc. of water, is well shaken and set aside for an hour to allow separation of inert, insoluble matter, after which it is filtered. The sugar is dissolved in the filtrate with the aid of only a gentle heat, to avoid loss of the volatile oils, and sufficient water is added to make up the required volume. The finished syrup contains very nearly 8 per cent. of alcohol derived from the fluidextracts, and therefore a less quantity of sugar than most other syrups. The present official formula differs from those formerly employed, in omitting guaiacum wood and pale-rose petals. Each Cc. of the finished syrup represents 0.200 Gm. of sarsaparilla, 0.015 Gm. each of senna and licorice root, and a trace each of the oils of gaultheria, anise, and sassafras.

Syrupus Scillæ (Syrup of Squill).—On account of the acetic acid present in the vinegar of squill this syrup should always be made in glass or porcelain vessels, and all contact with metal should be avoided. Each Cc. of the syrup represents 0.045 Gm. of squill.

Syrupus Scillæ Compositus (Compound Syrup of Squill).—Upon evaporation of the mixed fluidextracts of senega and squill nearly all the alcohol is dissipated and considerable insoluble matter is apt to separate, which, after the addition of the prescribed quantity of water, is mixed with purified talc and then filtered; if necessary, the liquid should be passed through the filter repeatedly until it runs clear. To the clear filtrate are added the antimony and potassium tartrate dissolved in hot water and the sugar, which latter is dissolved by agitation without heat, and sufficient water added to bring the volume up to the required measure. Each Cc. of the finished product represents 0.080 Gm. each of senega and squill, and contains 0.002 Gm. of antimony and potassium tartrate.

Syrupus Senegæ.—Syrup of senega, if made as now officially directed by mixing fluidextract of senega direct with syrup, has been found to keep as well as formerly when made by the more tedious process. Moreover, it may be made extemporaneously in small quantities as wanted. Each Cc. represents 0.20 Gm. of senega.

Syrupus Sennæ.—The official process for making syrup of senna yields a satisfactory product and does away with the tedious and undesirable method of infusion formerly employed. Being made with a fluidextract of senna prepared from leaves deprived of their resinous constituents, it is less apt to produce griping. Each Cc. of the syrup represents 0.25 Gm. of senna, and is flavored with oil of coriander.

Syrupus Tolutanus (Syrup of Tolu).—The official formula for this syrup yields a very satisfactory product. The small amount of alcohol allowed to remain aids in keeping more of the balsamic and odorous principles in solution. The finished syrup is a colorless liquid having a decided odor and taste of tolu. Each Cc. represents 0.01 Gm. of balsam of tolu.

Syrupus Zingiberis (Syrup of Ginger).—The addition of alcohol to the fluidextract of ginger is for the purpose of keeping more of the oleoresinous matter in solution in the aqueous liquid than would otherwise be the case. If carefully made, the official syrup has the characteristic aroma of ginger and a pleasant, slightly pungent taste. Each Cc. represents 0.03 Gm. of ginger.

CHAPTER XVII.

MUCILAGES, HONEYS, AND GLYCERITES.

MUCILAGES.

THE preparations recognized in the Pharmacopœia under this name are viscid, adhesive liquids formed by solution of mucilaginous principles in water ; with one exception they are unstable and readily undergo putrefactive changes in warm weather, hence they should be freshly prepared when wanted. The 4 official mucilages are those of acacia, sassafras pith, tragacanth, and elm.

Mucilago Acaciæ (Mucilage of Acacia).—The official directions require that acacia in small fragments be first washed with cold water, for the purpose of removing foreign matter often adhering to the outer surface. For every 340 Gm. of acacia used, 330 Cc. of lime-water are then added, and sufficient water to bring the total weight up to 1000 Gm. The official formula will produce quite a viscid liquid, containing 34 per cent. of acacia, each Cc. representing about 0.378 Gm., but the solution is weaker than the mucilage of the British and German pharmacopœias. Owing to the fact that the liquid becomes denser as solution progresses, agitation of the mixture will be found somewhat difficult, especially if large quantities are used, and it will be found more expedient to suspend the washed acacia in the mixture of water and lime-water, in a bag of loosely textured cloth, in a tightly closed wide-mouth jar, to be occasionally moved about in the liquid, so that fresh portions of the solvent may continually displace the solution formed and thus complete solution be more rapidly effected. The addition of lime-water is for the purpose of neutralizing the natural acidity of the acacia, the latter being chemically chiefly acid calcium arabate. Pieces of clear, white acacia should be selected for the mucilage, which, when made, should be preserved in completely filled bottles in a cool place.

Mucilago Sassafras Medullæ.—Mucilage of sassafras pith is made by macerating the pith in cold water for three hours and then straining ; the mixture should be kept in a covered vessel and occasionally stirred with a glass rod. Each Cc. represents 0.02 Gm. of sassafras pith.

Mucilago Tragacanthæ.—The official directions for preparing mucilage of tragacanth are, to add 6 Gm. of tragacanth to a boiling mixture of 18 Gm. of glycerin and 75 Cc. of water, and then macerate for twenty-four hours, with frequent stirring ; after the addition of sufficient water to bring the weight of the mixture up to

100 Gm. it is beaten to a uniform consistence and then expressed through muslin. Mucilage of tragacanth forms a somewhat opaque semiliquid jelly, and the presence of the glycerin prevents decomposition. Tragacanth is only partially soluble in water, but absorbs the latter and swells to a gelatinoid mass.

Mucilago Ulmi.—Mucilage of elm, although still recognized in the Pharmacopœia, is very rarely prepared by pharmacists; the official directions are to add 6 Gm. of bruised elm to 100 Cc. of water, and digest for one hour in a covered vessel on a water-bath. Mucilage of elm, like that of sassafras pith, spoils very readily, and should be freshly made when wanted.

HONEYS.

Clarified honey, or Mel Depuratum of the Pharmacopœia, is prepared by mixing honey with 2 per cent. of its weight of paper-pulp and heating the mixture on a water-bath as long as scum rises to the surface; the scum is carefully removed with a skimmer and sufficient distilled water added to restore loss by evaporation, after which the mixture is strained and 5 per cent. of its weight of glycerin is added to the strained liquid for the purpose of better preservation.

Medicated honeys are simply mixtures of clarified honey with certain medicinal agents, and are, as a rule, prepared extemporaneously.

Only one medicated honey is recognized in the Pharmacopœia, namely, **Mel Rosæ,** or honey of rose, which is made by mixing fluid extract of rose with clarified honey in such proportion that the finished product shall contain the astringent virtues of 12 Gm. of rose petals in every 100 Gm.; this is about equal to a mixture of 12 Cc. of fluid extract of rose with 64 Cc. of clarified honey.

GLYCERITES.

This valuable class of preparations consists of solutions of the medicinal agents in glycerin; they are permanent, and are readily miscible with water or alcohol. Of the official glycerites, 5 are liquid and 1 solid.

Glyceritum Acidi Tannici.—Although tannic acid is perfectly soluble in cold glycerin, the solution of so large a proportion as directed in the official glycerite is best effected by the aid of heat; contact with metallic vessels must be carefully avoided, and the tannic acid (20 Gm.) and glycerin (80 Gm.) should be intimately mixed with a glass rod before heat is applied. When solution is completed, a deep-green transparent liquid results, which should be strained while still warm through flannel or a pledget of cotton. Glycerite of tannic acid contains about 0.300 Gm. of tannic acid in each Cc., which is equal to about 120 grains in 1 fluidounce.

Glyceritum Amyli.—The official directions for preparing glycerite of starch are to stir 10 parts of starch with 10 parts of water and 80 parts of glycerin, to a homogeneous mixture, and then apply a gradually increased heat until a translucent jelly is formed. As starch usually occurs in lumps, it is necessary first to rub it in a mortar into a fine powder, which should be transferred to a porcelain capsule, and then mixed with the water and glycerin, so as to avoid loss, which is unavoidable if the mixture be made in the mortar; heat must be applied cautiously and the mixture *constantly* stirred with a thick glass rod or a wooden spatula, to avoid scorching and consequent discoloration. The liquid gradually thickens as the heat is increased, and the entire disappearance of white spots indicates perfect solution. The high heat, 140° C. (284° F.), indicated in the official formula is necessary to effect rupture of the starch granules, without which solution of the starch cannot take place; to insure uniform heating, wire gauze should invariably be interposed between the capsule and the flame. Glycerite of starch is hygroscopic, therefore it must be preserved in tightly closed jars, so as to avoid contact with air.

Glyceritum Boroglycerini.—The preparation of glycerite of boroglycerin, also known as glycerite of glyceryl borate and solution of boroglyceride, involves first the production of boroglycerin, or glyceryl borate, and secondly the solution of this compound in glycerin. When boric acid and glycerin are heated together to about 150° C. (302° F.) chemical action sets in, water being given off, while a new compound, glyceryl borate, is formed, which upon cooling is obtained as a transparent, almost colorless and very hygroscopic mass; the mixture must be frequently stirred to break up the constantly forming film, and care must be observed that the heat prescribed be neither exceeded nor continued longer than necessary, so as to avoid a yellowish or brownish coloration. Thirty-one parts of boric acid and 46 parts of glycerin will unite to form 50 parts of glyceryl borate; hence in the official process the reaction is known to be complete when the weight of the mixture has been reduced to 500 Gm.; then, while still hot, an equal weight of glycerin is added and thoroughly incorporated, thus making a 50 per cent. solution of boroglycerin. Each Cc. contains about 0.683 Gm. of boroglycerin, which is equal to about 312 grains in a fluidounce.

Glyceritum Ferri, Quininæ et Strychninæ Phosphatum (Glycerite of the Phosphates of Iron, Quinine, and Strychnine).—This glycerite has been introduced for the extemporaneous preparation of the syrup of the same name, since the latter preparation is prone to darken in the course of time. Soluble ferric phosphate (80 Gm.) having been dissolved in 200 Cc. of water with the aid of heat, 104 Gm. of quinine alkaloid and 0.8 Gm. of strychnine alkaloid mixed with 200 Cc. of phosphoric acid are next added, and then sufficient water to bring the volume of the liquid up to 500 Cc. The mixture is stirred until perfect solution has taken place, after which 500 Cc. of glycerin are added, and the whole then strained through a pledget of cotton. Each Cc. of the glycerite contains 0.104 Gm. of quinine, 0.0008 Gm. of strychnine, and 0.08 Gm. of soluble ferric phosphate.

Glyceritum Hydrastis (Glycerite of Hydrastis, also known as Glycerite of Golden Seal).—In the official process for this glycerite, 1000 Gm. of finely powdered hydrastis root are exhausted with alcohol by percolation. The alcohol is then nearly all recovered from the percolate by distillation, and the thick, concentrated liquid is poured into 500 Cc. of ice-cold water and set aside for 24 hours in a cold place. After filtration, sufficient water is passed through the filter to bring the volume of filtrate up to 500 Cc., and 500 Cc. of glycerin is then added. This preparation is of about the same strength as fluidextract of hydrastis, but is not standardized, each Cc. representing 1 Gm. of the root. It possesses the advantage of being miscible with water in all proportions without precipitation.

The object of removing the alcohol by distillation and then pouring the residue into ice-cold water, is to get rid of the soft resinous matter extracted from the root, which possesses no medicinal virtues and is immiscible with water.

Glyceritum Phenolis (Glycerite of Phenol, also known as Glycerite of Carbolic Acid).—The Pharmacopœia directs this glycerite to be made by mixing 1 volume of liquefied phenol with 4 volumes of glycerin. The official liquefied phenol, being made by adding 10 grammes of water to 90 grammes of melted phenol, should contain not less than 86.4 per cent. of absolute phenol, and hence each Cc. of the glycerite will contain 0.184 Gm. of pure phenol or carbolic acid. It is readily soluble in water.

Among the non-official glycerites there is one of considerable interest in pharmacy, namely, the glycerite of yolk of egg, also known as glyconin. It is made by dissolving 45 parts of yolk of egg in 55 parts of glycerin, and should be preserved in tightly-stoppered bottles so as to prevent the absorption of moisture from the air. In order to obtain a satisfactory preparation, the yolk of egg should be carefully separated from the albumen, and the membrane enclosing the yolk then ruptured, so that only the pure yolk may be weighed; the glycerin should be added gradually with constant trituration. As a fluidounce of this glycerite weighs about 640 grains, such a quantity may be made by using 288 grains of yolk of egg and 352 grains of glycerin. The chief use of glycerite of yolk of egg is as an emulsifying agent for fixed and volatile oils, 2½ fluidrachms being required for 1 fluidounce of the former, or ½ fluidounce of the latter.

CHAPTER XVIII.

ELIXIRS.

THE word "elixir" is said to be of ancient origin, and derived, according to Dr. Charles Rice, from two Arabic words, pronounced *al-iksir;* the Arabic *iksir* comes from the Greek ξήριον, meaning a dry powder, such as was used for dusting wounds. For a long time the word was applied by alchemists to the wonderful transformation powder used in the supposed conversion of base metals into silver and gold. Later on, the term was also applied to liquids, and used to designate certain compound tinctures for which rare medicinal properties were claimed. In this latter sense the term elixir is still used to some extent in Continental Europe, and, as a rule, such preparations are characterized by an unpleasant taste. In modern American pharmacy the word has come to mean an entirely different class of preparations, the distinguishing features of which are a pleasantly aromatic sweet taste, and the presence of alcohol varying in proportion from 20 to 25 per cent. by volume. Prior to 1865, only two elixirs of this kind were used to any extent in this country, namely, *Elixir of calisaya* and *Elixir of ammonium valerianate;* but through the efforts of enterprising manufacturers the list was rapidly augmented and reached its height between 1870 and 1875. A reaction, however, gradually set in, and at the present day many once-popular elixirs have fallen into disuse. There can be no doubt that a sweet, aromatic, and slightly alcoholic liquid forms a pleasant vehicle for many remedies, but the presence of 25 per cent. of alcohol may in some instances be positively injurious, and, moreover, the active ingredients are frequently present in such small quantities as to render the medicinal value of the preparation doubtful.

The American Pharmaceutical Association, in order to secure uniformity in the composition of the many elixirs dispensed by pharmacists, has published a series of 86 formulas for elixirs, in the *National Formulary.* This book first appeared in 1888, and a third edition, thoroughly revised, will be issued before the close of the present year (1905). Another series, containing about 275 formulas for elixirs and many valuable directions in manipulation, was published by J. U. Lloyd in 1892, under the title *Elixirs and Flavoring Extracts.* Many elixirs can be prepared extemporaneously by simple solution of the medicinal ingredient in the desired vehicle; as, for instance, the elixirs of the alkali bromides, citrates, salicylates, and hypophosphites, elixir of pyrophosphate of iron, elixir of gentian, both simple and ferrated, etc.

It is often desirable to impart color to an elixir, but since not all coloring agents are equally well suited for acid and alkaline liquids, it becomes necessary to exercise proper discretion. For acid or neutral liquids the *National Formulary* recommends either the simple or compound tincture of cudbear, the former for a bright-red and the latter for a brownish-red tint; of either tincture, 2 fluidrachms will suffice to color a pint of elixir. For alkaline liquids, such as elixir of ammonium valerianate, the coloring agent should be a solution of carmine, which is best prepared with the aid of ammonia-water; the *National Formulary* furnishes a satisfactory formula for the same.

The Pharmacopœia recognizes only three elixirs, namely, adjuvant elixir, aromatic elixir, and elixir of iron, quinine, and strychnine phosphates; the two former are chiefly intended as vehicles for the ready preparation of many others.

Elixir Adjuvans (Adjuvant Elixir).—This preparation, also known as aromatic elixir of licorice, is made by mixing 12 volumes of fluidextract of licorice with 88 volumes of aromatic elixir. It has a very sweet, aromatic taste, and is well adapted for disguising an unpleasant saline or bitter taste of drugs, but should never be used in connection with acid liquids, as these will cause precipitation.

Elixir Aromaticum (Aromatic Elixir, also known as Elixir of Orange and Simple Elixir).—The official directions for making this elixir are to mix compound spirit of orange, 12 Cc., with sufficient alcohol to produce 250 Cc.; to this solution are added syrup, 375 Cc., in divided portions, shaking after each addition, and afterward, in the same manner, 375 Cc. of distilled water. On account of the turbidity caused by the solution of the volatile oils, when mixed with the aqueous liquids, 30 Gm. of purified talc are added to the mixture, the whole well shaken and then filtered through paper, passing enough of a mixture of alcohol, 1 volume, and water, 3 volumes, through the filter to bring the volume up to 1000 Cc.

Elixir Ferri, Quininæ et Strychninæ Phosphatum; Elixir of Iron, Quinine, and Strychnine Phosphates.—The Pharmacopœia directs that quinine alkaloid, 8.75 Gm., and strychnine alkaloid, 0.275 Gm., be dissolved in alcohol, 60 Cc., phosphoric acid, 2 Cc., and aromatic elixir, 350 Cc., being added to the solution; ammonium carbonate, 9 Gm., is dissolved in acetic acid, 28.65 Gm., and sufficient distilled water added to make 50 Cc. of solution. The neutral solution of ammonium acetate is then mixed with the solution of the alkaloidal salts and sufficient aromatic elixir added to produce 880 Cc. of liquid. After dissolving soluble ferric phosphate, 17.5 Gm., in distilled water, 30 Cc., with the aid of heat, and rendering the solution exactly neutral by careful addition of ammonia-water, it is mixed with sufficient aromatic elixir to make 120 Cc. Finally, mix the two liquids, making 1000 Cc. of finished elixir.

If the official directions be carefully followed no difficulty will be experienced in obtaining a perfectly clear preparation, which is miscible with water in all proportions and keeps well at all seasons. The addition of ammonium acetate solution is essential to overcome the difficulty of precipitation, when the iron solution is mixed with the acid solution of the alkaloids. This elixir is prone to darken when exposed to light, and therefore should be preserved in a dark place and be always dispensed in dark-amber bottles. Each Cc. contains 0.0175 Gm. of soluble iron phosphate, 0.00875 Gm. of quinine, and 0.000275 Gm. of strychnine, both in the form of phosphates.

It is not within the scope of this work to furnish numerous formulas for elixirs, but there is one elixir deserving of special consideration, because it has been the source of much vexation to pharmacists; this is the elixir of pepsin, bismuth, and strychnine.

Elixir Pepsini, Bismuthi et Strychninæ; Elixir of Pepsin, Bismuth, and Strychnine.—One of the chief difficulties in connection with this elixir has been the preparation of a neutral liquid which shall permanently retain all three of the active ingredients in solution. Pepsin is active only in acid fluids, and its action is inhibited, and in the course of time destroyed, by alkalies. The official bismuth and ammonium citrate is not a very stable compound, and although perfectly soluble when freshly prepared, in plain water, it loses this property in time, owing to decomposition of the ammonium citrate; in alkaline liquids it retains its solubility, but an alkaline fluid will not only interfere with the pepsin, but may also throw the strychnine out of solution. The best that has been accomplished thus far has been a neutral solution of these three active ingredients—of doubtful stability, however, and likely to lose the bismuth salt by precipitation.

Since physicians desire and extensively prescribe the elixir of pepsin, bismuth, and strychnine, it becomes the duty of the pharmacist so to prepare it that a permanent solution shall result; this can only be done with a liquid of acid reaction. In 1888 the late R. Rother called attention to a permanent solution of bismuth and sodium tartrate of acid reaction, and suggested its use in place of the bismuth and ammonium citrate. The following formula has been found by many pharmacists to yield an unexceptionable preparation:

Take of

Pepsin in scales (U. S. P. standard)	64 grains.
Strychnine	2 "
Tartaric Acid	2 "
Distilled Water	4 fluidounces.
Glycerin	2 "
Glycerite of Bismuth and Sodium Tartrate	2 "
Caramel	4 drops.
Aromatic Elixir	8 fluidounces.

1. Dissolve the pepsin in a mixture of 1 fluidounce each of glycerin and water. 2. Dissolve the strychnine with the tartaric acid in 3 fluidounces of water, and add the remainder of the glycerin,

the bismuth solution, the caramel, and the aromatic elixir. 3. Finally, pour the pepsin solution into the other liquid. In place of the pepsin a corresponding quantity of glycerite of pepsin, *free from mineral acid*, may be used, and in that case the water and glycerin must be reduced accordingly.

This preparation contains $\frac{1}{2}$ grain of official pure pepsin, 2 grains of bismuth and sodium tartrate, and $\frac{1}{64}$ grain of strychnine, in each fluidrachm.

The glycerite of bismuth and sodium tartrate referred to in the above formula can be prepared as follows:

Take of

Bismuth Subnitrate	1142 grains.
Nitric Acid	19 fluidrachms.
Tartaric Acid	1720 grains.
Sodium Bicarbonate	1954 "
Glycerin	8 fluidounces.
Distilled Water	a sufficient quantity.

Dissolve the bismuth salt in the nitric acid, previously diluted with 10 fluidrachms of water; to the solution slowly add 16 fluidounces of water. Now add 860 grains of powdered tartaric acid, and then gradually 977 grains of sodium bicarbonate. Dilute the magma of bismuth tartrate with 32 fluidounces of water. Set the mixture aside for five or six hours and wash by decantation and repeated affusion of water, until all nitric acid has been removed; drain the precipitate on a paper filter. Mix 977 grains of sodium bicarbonate with 5 fluidounces of water and gradually add 860 grains of powdered tartaric acid, warming slightly to obtain a perfect solution. Transfer the precipitate of bismuth tartrate to the solution of sodium tartrate and stir until dissolved; filter the solution, add the glycerin, and evaporate it on a water-bath, or dilute it with water as may be necessary, so that the liquid shall measure 16 fluidounces. Each fluidrachm of this solution contains 16 grains of bismuth and sodium tartrate with an excess of sodium tartrate.

CHAPTER XIX.

SPIRITS OR ESSENCES.

In the Pharmacopœia the term "spiritus" is used to designate an alcoholic solution of volatile substances, chiefly volatile oils; in a few cases water also is added. Of the 20 spirits recognized in the Pharmacopœia, all but 5 can be conveniently prepared by the pharmacist, as they are quickly made and require only the ordinary apparatus usually found in a drugstore; as a rule, they are prepared by simple solution of the liquid or gaseous body in alcohol, although sometimes resort is had to distillation. Whenever volatile oils are used in the preparation of spirits, only the very best should be selected, as the value of the finished product depends entirely upon the quality of the oil; particular attention should be paid to those oils likely to have acquired a terebinthinate odor, such as the oils of juniper, lemon, nutmeg, and orange peel.

The following is a list of the official spirits, together with their composition:

Latin Name.	English Name.	Composition.
Spiritus Ætheris	Spirit of Ether	Ether $3\frac{1}{4}$ volumes, Alcohol $6\frac{3}{4}$ volumes.
Spiritus Ætheris Compositus	Compound Spirit of Ether (Hoffmann's Anodyne)	Ethereal Oil 1 volume, Ether 13 volumes, Alcohol 26 volumes.
Spiritus Ætheris Nitrosi	Spirit of Nitrous Ether (Sweet Spirit of Nitre)	An alcoholic solution of Ethyl Nitrite, containing, when freshly made, between 4 and 5 per cent. of the ethereal liquid.
Spiritus Ammoniæ	Spirit of Ammonia	An alcoholic solution of Ammonia containing 10 per cent. by weight of the gas.
Spiritus Ammoniæ Aromaticus	Aromatic Spirit of Ammonia	A hydro-alcoholic solution of normal Ammonium Carbonate, containing 70 per cent. by volume of Alcohol, 1 per cent. of Oil of Lemon, and $\frac{1}{10}$ per cent. each of Oil of Nutmeg and Oil of Lavender Flowers
Spiritus Amygdalæ Amaræ	Spirit of Bitter Almond (Essence of Bitter Almond)	Oil of Bitter Almond 1 volume, Alcohol 80 volumes, Distilled Water sufficient to make 100 volumes.
Spiritus Anisi	Spirit of Anise	Oil of Anise 1 volume, Alcohol 9 volumes.
Spiritus Aurantii Compositus	Compound Spirit of Orange	Oil of Orange Peel 20 volumes, Oil of Lemon 5 volumes, Oil of Coriander 2 volumes, Oil of Anise $\frac{1}{2}$ volume, Alcohol $72\frac{1}{2}$ volumes.
Spiritus Camphoræ	Spirit of Camphor	Camphor, 10 Gm., Alcohol sufficient to make 100 Cc. of solution.

Latin Name.	English Name.	Composition.
Spiritus Chloroformi	Spirit of Chloroform	Chloroform, 6 volumes; Alcohol, 94 volumes.
Spiritus Cinnamomi	Spirit of Cinnamon	Oil of Cinnamon, 1 volume; Alcohol, 9 volumes.
Spiritus Frumenti	Whiskey	An alcoholic liquid obtained by the distillation of the mash of fermented grain (usually of mixtures of corn, wheat, and rye).
Spiritus Gaultheriæ	Spirit of Gaultheria (Essence of Wintergreen)	Oil of Gaultheria, 1 volume; Alcohol, 19 volumes.
Spiritus Glycerylis Nitratis	Spirit of Glyceryl Trinitrate	An alcoholic solution of Glyceryl Trinitrate, containing 1 per cent. by weight of the substance.
Spiritus Juniperi	Spirit of Juniper	Oil of Juniper, 1 volume; alcohol, 19 volumes.
Spiritus Juniperi Compositus	Compound Spirit of Juniper	Oil of Juniper, 8 volumes; Oil of Caraway and Oil of Fennel, each 1 volume; Alcohol, 1400 volumes; Water sufficient to make 2000 volumes.
Spiritus Lavandulæ	Spirit of Lavender	Oil of Lavender Flowers, 1 volume; Alcohol, 19 volumes.
Spiritus Menthæ Piperitæ	Spirit of Peppermint (Essence of Peppermint)	Oil of Peppermint, 1 volume; Alcohol, 9 volumes. This spirit is colored green by peppermint herb.
Spiritus Menthæ Viridis	Spirit of Spearmint (Essence of Spearmint)	Oil of Spearmint, 1 volume; Alcohol, 9 volumes. This spirit is colored green by spearmint herb.
Spiritus Vini Gallici	Brandy	An alcoholic liquid obtained by the distillation of the fermented unmodified juice of fresh grapes.

SPECIAL REMARKS.

Spiritus Ætheris Compositus.—Commercial Hoffmann's anodyne varies greatly in composition, and is probably never identical with the official spirit—in fact, manufacturers do not claim this to be the case; hence the necessity for discrimination between the two preparations when physicians prescribe compound spirit of ether. The commercial varieties of Hoffmann's anodyne are often obtained as by-products in the rectification of ether, and consist of mixtures of heavy and light oil of wine, ether, alcohol, and water, brought up to a certain arbitrary standard, varying with different manufacturers.

Spiritus Ætheris Nitrosi.—This preparation is a very unstable solution, at least as far as the proportion of active ingredients is concerned; even under the most favorable conditions it deteriorates; to retard this change as far as possible, the spirit should be preserved in small, well-stoppered bottles, in a cool, dark place. Spirit of nitrous ether should be purchased in original packages, and never in bulk drawn from carboys.

The chemical reactions involved in the manufacture of this spirit will be explained elsewhere, as also the official method of determining its quality.

Spiritus Ammoniæ.—The object of directing the use of alcohol recently distilled and preserved in glass, is to avoid discoloration of the liquid, which is likely to occur if ammonia gas be dissolved in alcohol kept in barrels and containing organic impurities. Spirit of ammonia is of the same strength as official ammonia water, and is intended to be used in cases where the aqueous solution is inadmissible.

Spiritus Ammoniæ Aromaticus.—Ammonia water is used in connection with official ammonium carbonate, for the purpose of converting the latter into the normal salt, as this alone is soluble in the alcoholic liquid; in order to complete the change, it is advisable to let the aqueous solution stand for twelve or twenty-four hours before adding to it the mixture of oils and alcohol. Aromatic spirit of ammonia is of faint color when freshly prepared, but gradually becomes darker.

Spiritus Frumenti.—Whiskey, as recognized by the Pharmacopœia, should contain from 44 to 55 per cent. by volume of alcohol, which is readily ascertained by aid of the alcoholometer described on page 64. 100 Cc. of whiskey when evaporated to dryness should not yield more than 0.5 Gm. of residue.

Spiritus Glycerylis Nitratis.—Spirit of glyceryl trinitrate was formerly officially recognized as spirit of glonoin, a name originally given to the preparation by the homœopaths. It is also sometimes called spirit of nitroglycerin and spirit of trinitrin, but these names are improper and should not be used. The spirit should be transported in well-stoppered tin cans and kept in a cool place remote from lights and fire. If through accident some of the spirit be spilled, especially a large quantity, a solution of potassium hydroxide should be at once poured over it to effect decomposition, and thus avert the danger which would arise from evaporation of the alcohol and leaving the explosive glyceryl trinitrate as a residue.

Spiritus Vini Gallici.—Official brandy should be at least four years old, and contain from 46 to 55 per cent. by volume of alcohol; the older the brandy the finer is its quality. 100 Cc. of brandy upon evaporation to dryness should not yield more than 0.5 Gm. of residue.

CHAPTER XX.

TINCTURES.

TINCTURE is the name applied to solutions of non-volatile or only partially volatile substances, in liquids other than simple water or glycerin, and which invariably contain alcohol; solutions of volatile substances in alcohol are always termed spirits or essences. While tinctures are usually assumed to be solutions of vegetable principles, this is not the case in all the official tinctures; two of these, the tinctures of iodine and ferric chloride, are solutions of inorganic substances, and must also be classed as exceptions to the rule that tinctures are solutions of non-volatile substances. The menstruum or solvent used in the preparation of tinctures may be simply alcohol, various mixtures of alcohol and water, or of alcohol, glycerin, and water, ammoniated alcohol in the form of aromatic spirit of ammonia, and mixtures of alcohol and ether; according as these different menstrua are employed, tinctures are divided into groups designated as alcoholic, hydro-alcoholic, ammoniated, and ethereal tinctures, respectively. Ethereal tinctures are not recognized in the U. S. Pharmacopœia, but are employed to some extent in Europe.

The Pharmacopœia recognizes 64 tinctures, of which 18 are made with alcohol alone, 44 with a hydro-alcoholic menstruum, and 2 with ammoniated alcohol; from this it is seen that the tendency is in the direction of weaker alcohol, and many tinctures formerly made with alcohol exclusively, are now found equally efficient and permanent when made with a mixture of alcohol and water. The valuable solvent and preservative properties of alcohol have been explained in a preceding chapter; these are retained in the various hydro-alcoholic mixtures, in which the proportions of alcohol and water are so adjusted that complete extraction of the valuable constituents of the drug is insured as well as permanence of the solution; the solution of much inert and unstable matter is likewise thus avoided. Tinctures made with weak alcohol are also more readily miscible with aqueous liquids—a point often of great value in dispensing medicines. The addition of glycerin to the menstruum is frequently desirable, to facilitate the perfect extraction of astringent and other principles, and to prevent subsequent changes in the finished tincture, due to atmospheric influences, which cause gelatinization of the solution or deposit of unsightly precipitates.

The following is a list of the official tinctures containing glycerin: Camphorated tincture of opium, 4 per cent.; compound tincture of cardamom, 5 per cent.; tincture of cinchona, 7.5 per cent.; compound tincture of cinchona, 7.5 per cent.; tincture of cinnamon, 7.5 per cent.; tincture of kino, 15 per cent.; tincture of nutgall, 10 per cent.; tincture of lactucarium, 25 per cent.; tincture of rhubarb, 10 per cent.; aromatic tincture of rhubarb, 10 per cent.

Tinctures are, as a rule, prepared by percolation, except in the case of a few resins, balsams, gum-resins, and extractive drugs, for which maceration has proved more satisfactory. The process of percolation has been fully described on page 130 *et seq.*, as well as the precautions necessary to insure perfect extraction of drugs. The great advantages to be derived from a proper moistening and preliminary maceration of the drug have been pointed out in the chapter on Percolation. The value of this mode of solution cannot be overestimated in the preparation of tinctures, and as the amount of available menstruum is ample, complete exhaustion of the drug will have been effected before all the solvent has passed through; the objection urged that menstruum is retained by the marc can be easily overcome (see page 142), and is but trifling as compared with the gain in time and in the perfect, clear solution at once obtained.

In the case of tinctures to be made by percolation, the Pharmacopœia, with very few exceptions, directs that the powder, having been moistened with the prescribed quantity of menstruum, shall be set aside without being compressed for a period varying from 3 to 24 hours before it is packed in the percolator. Having been properly packed and saturated with menstruum, it is allowed to macerate for 24 hours (in a few cases 48 hours) before percolation is started. This preliminary treatment is intended to insure more thorough penetration of the cellular tissue by the menstruum, and has been found very effectual in furthering the extraction of the soluble principles sought.

Whenever tinctures are to be made by maceration, the Pharmacopœia directs that about three-fourths of the total menstruum be added to the powdered drugs and the mixture set aside in a shady place at a temperature of about 15° to 20° C. (59°–68° F.) with occasional agitation. The length of time required for maceration varies for different drugs, from 2 to 14 days, and is specifically stated in each official formula. At the expiration of the specified time the mixture is filtered through absorbent cotton, and when the liquid has all drained off sufficient menstruum is passed through the dregs to bring the volume up to the required measure.

Of the 64 official tinctures, 39, or more than one-half of the whole number, are directed to be made by percolation, 20 by maceration, 4 by direct solution, and 1 by decoction and subsequent concentration. In the pharmacopœial titles of tinctures, the names of the drugs furnishing the active ingredients are indicated in all but

10; of these, 6 are officially designated as *compound tinctures*, namely: the *compound tinctures* of *benzoin*, *cardamom*, *cinchona*, *gambir*, *gentian*, and *lavender*. In the remaining 4 titles, only the name of the chief ingredient is mentioned; as *tincture of aloes*, *camphorated tincture of opium*, *tincture of rhubarb*, and *aromatic tincture of rhubarb*.

Upon exposure to air and light, tinctures, like all vegetable solutions, are prone to undergo change, and should, therefore, be kept in well-closed containers, in places not exposed to direct sunlight; extremes of temperature are equally hurtful on account of possible change in the menstruum. Fortunately, the deposits formed in tinctures consist, as a rule, only of inert extractive matter, which may be removed by filtration.

The following table shows the composition and strength of the official tinctures, as well as the fineness of powder and the menstruum used in their preparation.

TABLE OF OFFICIAL TINCTURES ARRANGED ALPHABETICALLY.

Tinctures Made by Percolation.

Official Name.	Quantity of drug used for 1000 Cc. of tincture.	Fineness of powder.	Menstruum.	Quantity of menstruum to moist'n drug.	Degree of Packing
Tinctura—					
Aconiti	Aconite 100 Gm.	No. 60	Alcohol 7 vols. Water 3 "	40 Cc.	Firm.
Aurantii Amari	Bitter Orange Peel 200 "	" 40	Alcohol 6 " Water 4 "	80 "	"
Belladonnæ Fol.	Belladonna Leaves 100 "	" 60	Dil. Alcohol	40 "	"
Calendulæ . . .	Calendula 200 "	" 20	Alcohol	80 "	"
Calumbæ	Calumba 200 "	" 20	Alcohol 6 vols. Water 4 "	100 "	Moderate.
Cannabis Indicæ	Indian Cannabis 100 "	" 40	Alcohol	50 "	Firm.
Cantharidis . . .	Cantharides 100 "	" 60	Alcohol	35 "	"
Capsici	Capsicum 100 "	" 50	Alcohol 95 " Water 5 "	35 "	"
Cardamomi . . .	Cardamom 200 "	" 30	Dil. Alcohol	80 "	"
Cimicifugæ . . .	Cimicifuga 200 "	" 40	Alcohol	60 "	"
Cinchonæ	Cinchona 200 "	" 60	Alcohol 67.5 vols. Water 25 " Glycerin 7.5 "	80 "	"
Cinchonæ Composita .	Red Cinchona 100 " Bitter Orange Peel 80 " Serpentaria 20 "	" 60	Alcohol 67.5 " Water 25 " Glycerin 7.5 "	80 "	"
Cinnamomi . . .	Saigon Cinnamon 200 "	" 50	Alcohol 67.5 " Water 25 " Glycerin 7.5 "	80 "	"
Colchici Seminis	Colchicum Seed 100 "	" 50	Alcohol 6 " Water 4 "	40 "	"
Digitalis	Digitalis 100 "	" 60	Dil. Alcohol	40 "	"
Gallæ	Nutgall 200 "	" 40	Alcohol 9 vols. Glycerin 1 vol.	0 "	
Gelsemii	Gelsemium 100 "	" 60	Alcohol 65 vols. Water 35 "	35 "	"
Gentianæ Composita .	Gentian 100 " Bitter Orange Peel 40 " Cardamon 10 "	" 40	Alcohol 6 " Water 4 "	60 "	"
Hydrastis	Hydrastis 200 "	" 60	Alcohol 65 " Water 35 "	60 "	"

TABLE OF OFFICIAL TINCTURES ARRANGED ALPHABETICALLY.—*Continued.*

Tinctures Made by Percolation.

Official Name.	Quantity of drug used for 1000 Cc. of tincture.	Fineness of powder.	Menstruum.	Quantity of menstruum to moist'n drug.	Degree of Packing
Tinctura—					
Hyoscyami . . .	Hyoscyamus 100 "	" 60	Dil. Alcohol	40 "	Firm.
Krameriæ . . .	Krameria 200 "	" 40	Dil. Alcohol	80 "	"
Lactucarii . . .	Lactucarium 500 " (the drug is mixed with sand and treated twice with benzin before percolation)	. . .	Alcohol 50 vols. Water 20 " Glycerin 25 " afterward Dil. Alcohol	0 "	Moderate.
Lobeliæ	Lobelia 100 Gm.	" 50	Dil. Alcohol	40 "	Firm.
Opii	Granulated Opium 100 "	. . .	Dil. Alcohol		
Opii Deodorati .	Granulated Opium 100 "	. . .	Water	Finished product contains 20 per cent. alcohol	
Physostigmatis .	Physostigma 100 "	" 50	Alcohol	40 Cc.	Firm.
Pyrethri	Pyrethrum 200 "	" 50	Alcohol	80 "	"
Quassiæ	Quassia 200 "	" 50	Alcohol 35 " Water 65 "	60 "	"
Rhei	Rhubarb 200 " Cardamom 40 "	" 40	Alcohol 5 " Water 4 " Glycerin 1 vol.	90 "	"
Rhei Aromatica	Rhubarb 200 " Saigon Cinnamon 40 " Cloves 40 " Nutmeg 20 "	" 40	Alcohol 5 vols. Water 4 " Glycerin 1 vol. afterward Dil. Alcohol	90 "	"
Sanguinariæ . .	Sanguinaria 100 "	" 60	Alcohol 6 vols. Water 4 " Acetic Acid 2 p.c.	50 "	"
Serpentariæ . .	Serpentaria 200 "	" 50	Alcohol 65 vols. Water 35 "	60 "	"
Stramonii . . .	Stramonium 100 "	" 60	Dil. Alcohol	40 "	"
Strophanthi . .	Strophanthus 100 "	" 60	Alcohol 65 " Water 35 "	50 "	"
Valerianæ . . .	Valerian 200 Gm.	" 60	Alcohol 75 vols. Water 25 "	60 Cc.	"
Valerianæ Ammoniata	Valerian 200 "	" 60	Aromatic Spirit of Ammonia.	60 "	"
Vanillæ	Vanilla 100 "	. . .	Alcohol 65 vols. Water 35 "		
Veratri	Veratrum 100 "	" 60	Alcohol	40 "	"
Zingiberis . . .	Ginger 200 "	" 50	Alcohol	60 "	"

Tinctures Made by Solution.

Official Name.	Quantity of drug used for 1000 Cc. of tincture.	Menstruum.
Tinctura—		
Ferri Chloridi	Solution of Ferric Chloride . . 350 Cc.	Alcohol.
Ipecacuanhæ et Opii .	Fluidextract of Ipecac . . . . . 100 " Tincture of deodorized Opium . 1000 "	Dil. Alcohol.
Iodi	Iodine . . . . 70 Gm. Potassium Iodide . . . . 50 "	Alcohol.
Nucis Vomicæ	Extract of Nux Vomica . . . . . 20 "	Alcohol 750 Cc. Water 250 "

Tinctures Made by Maceration.

Official Name.	Quantity of drug used for 1000 Cc. of tincture.	Menstruum.	Length of time of macerati'n.
Tinctura—			
Aloes	Purified Aloes, No. 40 powder, 100 Gm. Licorice Root, No. 40 powder, 200 "	Dil. Alcohol.	7 days.
Aloes et Myrrhæ . .	Purified Aloes, No. 40 powder, 100 " Licorice Root, No. 40 powder, 100 " Myrrh, No. 40 powder, 100 "	Alcohol, 750 Cc. Water, 250 Cc.	7 "
Asafœtidæ	Asafetida, well bruised, 200 "	Alcohol.	3 "
Arnicæ	Arnica, No. 20 powder, 200 "	Dil. Alcohol.	4 "
Aurantii Dulcis , . . .	Sweet Orange Peel, shredded, 500 "	Alcohol.	2 "
Benzoini	Benzoin, No. 40 powder, 200 "	Alcohol.	3 "
Benzoini Composita .	Benzoin, No. 40 powder, 100 " Purified Aloes, No. 40 powder, 20 " Storax, 80 " Balsam of Tolu, 40 "	Alcohol.	3 "
Cardamomi Composita	Cardamom, No. 40 powder, 25 " Saigon Cinnamon, No. 40 powder, 25 " Caraway, No. 40 powder, 12 " Cochineal, No. 40 powder, 5 "	Dil. Alcohol, 950 Cc. Glycerin, 50 Cc.	7 "
Gambir Composita . .	Gambir, No. 50 powder, 50 " Saigon Cinnamon, No. 50 powder, 25 "	Dil. Alcohol.	2 "
Guaiaci	Guaiac, No. 40 powder, 200 "	Alcohol.	3 "
Guaiaci Ammoniata .	Guaiac, No. 40 powder, 200 "	Aromatic Spirit of Ammonia.	3 "
Kino	Kino, 50 "	Glycerin, 150 Cc. Water, 200 Cc. Alcohol, 650 Cc.	
Lavandulæ Composita	Saigon Cinnamon, No. 50 powder, 20 " Cloves, No. 50 powder, 5 " Nutmeg, No. 50 powder, 10 " Red Saunders, No. 50 powder, 10 " Oil of Lavender, 8 Cc. Oil of Rosemary, 2 "	Alcohol, 750 Cc. Water, 250 Cc.	3 "
Limonis Corticis . . .	Lemon Peel, shredded, 500 Gm.	Alcohol.	2 "
Moschi	Musk, 5 "	Dil. Alcohol.	7 "
Myrrhæ	Myrrh, moderately coarse powder, 200 "	Alcohol.	3 "
Opii Camphorata . . .	Opium, powdered, 4 " Benzoic Acid, 4 " Camphor, 4 " Oil of Anise, 4 Cc. Glycerin, 40 "	Dil. Alcohol.	3 "
Scillæ	Squill, No. 20 powder, 100 Gm.	Alcohol, 750 Cc. Water, 250 Cc.	4 "
Tolutana	Balsam of Tolu, 200 "	Alcohol.	Until dissolved.
Tincturæ Herbarum Recentium	Fresh Herbs, bruised, 500 "	Alcohol.	14 days.

Tincture Made by Decoction.

Official Name.	Quantity of drug used for 1000 Cc. of tincture.	Menstruum.
Tinctura Quillajæ	Quillaja, coarsely ground, 200 Gm.	Boiling water; the decoction is preserved by alcohol, of which the finished tincture contains 35 per cent.

The strength of the tinctures of the U. S. Pharmacopœia varies from 1.6 to 50 Gm. of drug, being in the majority of cases 10 or 20 Gm. for every 100 Cc. of finished product. The British Pharmacopœia of 1898 offers duplicate formulas for the preparation of its tinctures; in one, imperial weights and measures are employed, in the other, metric weights and measures. The strength of the official British tinctures varies from ¼ ounce to 5 ounces of drug in 1 imperial pint (20 fluidounces) of finished product, or from 12.5 Gm. to 250 Gm. in 1000 Cc.; of the 68 tinctures recognized, 29 are directed to be made by percolation and 26 by maceration. The French and German Pharmacopœias direct their tinctures to be prepared by maceration, and, almost without exception, of such strength that 1 part of drug is represented by about 5 or 10 parts of tincture by weight. While the difference in strength between our own and the British tinctures is in the majority of cases of no great importance, it is quite marked in a few tinctures, and should be borne in mind when filling British prescriptions; thus, our tincture of aconite is about twice as strong as the British tincture, our tincture of cantharides is 8 times as strong, our tincture of iodine nearly 3 times as strong, our tincture of strophanthus 4 times as strong, and our tincture of opium 50 per cent. stronger. The following table represents a classification of the official tinctures based upon the amount of drug represented in each liter:

TABLE OF OFFICIAL TINCTURES ARRANGED ACCORDING TO STRENGTH.

0.07 Gm. of mydriatic alkaloids in 1000 Cc.	Tinctura Hyoscyami.
0.14 Gm. of ether-soluble alkaloids in 1000 Cc.	" Physostigmatis.
0.30 Gm. of mydriatic alkaloids in 1000 Cc.	" Stramonii.
0.35 Gm. of mydriatic alkaloids in 1000 Cc.	" Belladonnæ.
0.45 Gm. of aconitine in 1000 Cc.	" Aconiti.
0.50 Gm. of colchicine in 1000 Cc.	" Colchici Seminis.
1.00 Gm. of strychnine in 1000 Cc.	" Nucis Vomicæ.
4.00 Gm. of hydrastine in 1000 Cc.	" Hydrastis.
7.50 Gm. of anhydrous ether-soluble alkaloids	" Cinchonæ.
12–12.5 Gm. of crystallizable morphine in 1000 Cc.	" Opii.
	" Opii Deodorati.
16 Gm. of drug in 1000 Cc.	" Opii Camphorata.
50 Gm. of drug in 1000 Cc.	" Kino.
	" Moschi.
55 Gm. of drug in 1000 Cc.	" Lavandulæ Composita.
67 Gm. of drug in 1000 Cc.	" Cardamomi Composita.
75 Gm. of drug in 1000 Cc.	" Gambir Composita.
100 Gm. of drug in 1000 Cc.	" Cantharidis.
	" Cannabis Indicæ.
	" Capsici.
	" Digitalis.
	" Gelsemii.
	" Lobeliæ.
	" Sanguinariæ.
	" Scillæ.
	" Strophanthi.
	" Vanillæ.
	" Veratri.
120 Gm. of drug in 1000 Cc.	" Iodi.

TABLE OF OFFICIAL TINCTURES ARRANGED ACCORDING TO STRENGTH.—*Continued.*

132.8 Gm. of anhydrous salt in 1000 Gm. . . .	Tinctura Ferri Chloridi.
150 Gm. of drug in 1000 Cc.	“ Gentianæ Composita.
200 Gm. of drug in 1000 Cc.	“ Arnicæ.
	“ Asafœtidæ.
	“ Aurantii Amari.
	“ Benzoini.
	“ Calendulæ.
	“ Calumbæ.
	“ Cardamomi.
	“ Cimicifugæ.
	“ Cinchonæ Composita.
	“ Cinnamomi.
	“ Gallæ.
	“ Guaiaci.
	“ Guaiaci Ammoniata.
	“ Ipecacuanhæ et Opii.
	“ Krameriæ.
	“ Myrrhæ.
	“ Pyrethri.
	“ Quassiæ.
	“ Quillajæ.
	“ Serpentariæ.
	“ Tolutana.
	“ Valerianæ.
	“ Valerianæ Ammoniata.
	“ Zingiberis.
240 Gm. of drug in 1000 Cc.	“ Benzoini Composita.
	“ Rhei.
300 Gm. of drug in 1000 Cc.	“ Aloes.
	“ Aloes et Myrrhæ.
	“ Rhei Aromatica.
500 Gm. of drug in 1000 Cc.	“ Aurantii Dulcis.
	“ Lactucarii.
	“ Limonis Corticis.
	Tincturæ Herbarum Recentium.

SPECIAL REMARKS.

Tinctura Aconiti; Tincture of Aconite.—This important tincture requires care in its preparation, as the drug is not easily exhausted. The drug should contain not less than 0.5 per cent. of aconitine when tested by the official method of assay, and percolation should be conducted at the rate of not over 10 drops per minute. Each Cc. of the finished product should contain 0.00045 Gm. of aconitine.

Tincture of aconite has a yellowish-brown color, and on the addition of water becomes turbid from the precipitation of resin. On account of its potent character it should never be dispensed except on physicians' prescriptions. The present tincture of aconite is very much weaker than that heretofore officially recognized, which represented 0.35 Gm. of aconite root in each Cc., and hence the dose is proportionately larger.

Fleming's tincture of aconite, which is still occasionally prescribed, is about ten times as strong as the official tincture. It is made by percolating aconite root (1920 grains) with sufficient alcohol to obtain 6 fluidounces of tincture.

Tinctura Aloes; Tincture of Aloes.—Although the Pharmacopœia directs this tincture to be prepared by maceration, it can be made as well by percolation, owing to the presence of the large quantity of licorice root, which latter at the same time materially modifies the bitter taste of the tincture. Tincture of aloes has a dark blackish-brown color.

Tinctura Aloes et Myrrhæ; Tincture of Aloes and Myrrh.—This tincture differs from the preceding in color, odor, and taste, on account of the myrrh present, and for the same reason is precipitated when added to water. It was at one time prescribed as *elixir proprietatis*, but is little used now.

Tinctura Arnicæ; Tincture of Arnica.—Arnica flowers in No. 20 or 30 powder, if thoroughly moistened, firmly packed, and saturated with menstruum, and then allowed to macerate for 48 hours, can be exhausted by percolation as well as by the more tedious official process of repeated maceration and expression. The tincture has a yellowish-brown color and the characteristic odor of the flowers.

Tinctura Asafœtidæ; Tincture of Asafetida.—Since much of the commercial asafetida is of inferior quality, only select gum-resin, containing not less than 50 per cent. of matter soluble in alcohol should be used for making the tincture, the value of the drug residing in the resinous constituents. Tincture of asafetida has a brownish-red color and the disagreeable odor of the drug. When added to aqueous fluids it forms milky mixtures, owing to precipitation of resin.

Tinctura Aurantii Amari; Tincture of Bitter Orange Peel.—This tincture should not be confounded with the next following tincture. It is made by exhausting the rind of the unripe bitter orange with a hydro-alcoholic menstruum, and has a greenish-brown color and a bitter taste.

Tinctura Aurantii Dulcis; Tincture of Sweet Orange Peel.—Only the fresh peel from sweet oranges should be used for this tincture, and instead of the more tedious shredding, it may be grated, the outer rind, rich in oil cells, alone being used. The present official tincture is more than twice as strong as the former. It has a deep reddish-yellow color and a strong fragrant odor, and is superior to a solution of oil of orange peel in alcohol as a flavoring agent. The tincture of orange of the British Pharmacopœia closely resembles this preparation in color and odor, but is made from the fresh peel of bitter oranges.

Tinctura Belladonnæ; Tincture of Belladonna Leaves.—The present tincture of belladonna is about one-third weaker than that formerly official. Owing to the variation in alkaloidal content of commercial belladonna leaves, it should be made from assayed leaves containing not less than 0.35 per cent. of alkaloids. If the official directions be followed, the drug is not difficult to exhaust, the resulting tincture having a greenish-brown color and a heavy narcotic odor. Each Cc. of the tincture should contain 0.00035 Gm. of mydriatic alkaloids. The British tincture of belladonna is made from the root and is standardized to contain 0.0005 Gm. of alkaloids in each Cc., and is therefore about half again as strong as our own tincture.

Tinctura Benzoini Composita; Compound Tincture of Benzoin.—This tincture is intended to take the place of numerous semi-proprietary preparations formerly much used, such as Wade's Vervain's, Saint Victor's Jesuit's, Friars', Turlington's, Persian, and Swedish Balsam. It is of a deep red-brown color, has a rather pleasant balsamic odor, and yields with water a reddish-white opaque mixture having an acid reaction.

Tinctura Cannabis Indicæ; Tincture of Indian Hemp.—The present official tincture is about one-third weaker than the former, and only about one-fourth as strong as the tincture of the British Pharmacopœia, which latter is made by dissolving 50 Gm. of extract of Indian cannabis in sufficient alcohol to make 1000 Cc. of tincture, good Indian cannabis yielding about 12½ per cent. of extract. The tincture has a deep-green color and a disagreeable heavy odor. It is precipitated by addition of water.

Tinctura Cinchonæ; Tincture of Cinchona.—This preparation should be made from assayed cinchona bark yielding not less than 4 per cent. of anhydrous ether-soluble alkaloids, and should contain 0.0075 Gm. of these alkaloids in each Cc. It is richer in alkaloids than the tincture next following and should not be confounded with the same.

Tinctura Cinchonæ Composita; Compound Tincture of Cinchona.—Although the Pharmacopœia directs that this tincture shall be made from assayed red cinchona bark yielding not less than 5 per cent. of total anhydrous alkaloids, no requirement is made for definite alkaloidal content for the finished product. The tincture has a brownish-red color and a very bitter taste. If the drugs have been carefully exhausted, it will contain about 0.005 Gm. of cinchona alkaloids in each Cc. In this as well as in the preceding tincture the use of a strongly alcoholic menstruum with the addition of glycerin prevents the deposit of cinchona red, an oxidation product of cincho-tannic acid.

Tinctura Colchici Seminis; Tincture of Colchicum Seed.—The present tincture is about one-third weaker than heretofore, and should contain in each Cc. 0.0005 Gm. of colchicine, when assayed by the official method. The Pharmacopœia directs that it shall be made from colchicum seed containing not less than 0.55 per cent. of alkaloid.

Tinctura Ferri Chloridi; Tincture of Ferric Chloride.—Although the official formula at first glance seems to direct an increased quantity of solution of ferric chloride, the actual strength of the present tincture is about the same as formerly, since the official solution contains only 29 per cent. of anhydrous ferric chloride as against 37.8 per cent. heretofore. When an acid solution of chloride of iron is mixed with alcohol, as in the official process, contraction of volume occurs, and a subsequent addition of alcohol is necessary to bring the finished product up to the required volume; furthermore, an ethereal odor is gradually developed, due to chemical reaction between the acid and alcohol. The pharmacopœial direction to allow the mixture to stand at least 3 months before using, is intended to insure uniformity by bringing all changes to completion, but it is questionable whether the time stated is sufficient for this purpose. When the tincture is exposed to light, the ferric chloride is slowly reduced to ferrous salt, the color of the solution changing at the same time, and hence it should be kept protected from light.

Tinctura Gambir Composita; Tincture of Gambir.—This tincture is intended to take the place of the former compound tincture of catechu, and has been reduced to one-half the strength. True catechu not being available in the market any longer, gambir, also known as pale catechu, is now used in its stead. The tincture has a reddish-brown color and a strongly astringent taste.

Tinctura Hydrastis; Tincture of Hydrastis.—Instead of diluted alcohol, a stronger alcoholic menstruum is now used to facilitate extraction of the drug. The tincture is required to contain 0.004 Gm. of hydrastine in each Cc. and must be standardized accordingly. It is not miscible with aqueous liquids without precipitation, on account of the resinous matter present.

Tinctura Hyoscyami; Tincture of Hyoscyamus.—The present official tincture is about one-third weaker than formerly. Hyoscyamus is very variable in its alkaloidal content and much of the commercial article is of poor quality, hence an assayed drug should be used for making the tincture. Each Cc. of the tincture is required to contain 0.00007 Gm. of mydriatic alkaloids.

Tinctura Iodi; Tincture of Iodine.—The present official formula differs from former directions in ordering the addition of potassium iodide, partly for the purpose of retarding the formation of hydriodic acid and partly to prevent precipitation when the tincture is mixed with water. Each Cc. contains 0.05 Gm. of potassium iodide, and when assayed should show the presence of about 0.0686 Gm. of iodine. It is better to make tincture of iodine in small quantities and protect it against light and air.

Tinctura Ipecacuanhæ et Opii; Tincture of Ipecac and Opium.—This preparation may be looked upon as a liquid form of Dover's powder, as it represents in each Cc. the equivalent of 0.10 Gm. each of ipecac and opium. The concentration of the tincture of deodorized opium is necessary to permit the introduction of the fluidextract of ipecac, the original volume being restored by addition of diluted alcohol; any precipitate formed consists of inert matter, and is removed by filtration.

Tinctura Kino; Tincture of Kino.—In order to better protect this tincture against gelatinization it should be preserved in a cool place, in well-stoppered small vials of 1- or 2-oz. capacity, thus obviating frequent exposure to air.

Tinctura Lactucarii; Tincture of Lactucarium.—The object of treating the lactucarium with purified petroleum benzin is to remove lactucerin and caoutchouc-like matters, the active principles, lactucin, lactucic acid, and lactucopicrin not being affected by that liquid. In order finally to get rid of all benzin odor, the residue should be dried in a current of warm air. The subsequent percolation of the powder mixed with sand presents no difficulty, the active principles being all soluble in diluted alcohol, but in order to insure complete exhaustion, the percolate should be collected very slowly. If carefully made the tincture is miscible with glycerin and syrup without precipitation.

Tinctura Limonis Corticis; Tincture of Lemon Peel.—This tincture is of the same strength as the tincture of sweet orange peel and made in the same manner. It is intended to replace the spirit of lemon of former pharmacopœias, and is of much finer flavor than the latter.

Tinctura Nucis Vomicæ; Tincture of Nux Vomica.—Being made by dissolving a specified quantity of standardized extract of nux vomica in the prescribed menstruum, this tincture should be of uniform strength at all times. The alkaloidal strength, which heretofore was fixed at 0.003 Gm. of total alkaloids for each Cc. of finished product, has been changed to 0.001 Gm. of strychnine. The official tincture has a yellowish color and a very bitter taste, and becomes opalescent when mixed with water. It is about one-third weaker than formerly and less than one-half as strong as the tincture of the British Pharmacopœia, which latter contains 0.025 Gm. of strychnine in each Cc.

Tinctura Opii; Tincture of Opium.—Opium readily yields its active constituents to water, and the preliminary treatment of the coarse powder with hot water is intended to facilitate complete exhaustion by the hydro-alcoholic menstruum used subsequently. The present tincture is slightly weaker than that formerly official, and should contain in each Cc. not less than 0.012 nor more than 0.0125 Gm. of crystallizable morphine. It has a deep reddish-brown color and the characteristic narcotic odor and bitter taste of opium. The British tincture is only two-thirds as strong as our own. The name *laudanum* is officially applied to tincture of opium by the Pharmacopœia, and, owing to the great abuse to which it is put by being given indiscriminately to the public, it should be dispensed only on physicians' prescriptions or to persons known not to be addicted to the use of opium.

Tinctura Opii Deodorati; Tincture of Deodorized Opium.—In order to deprive opium of its peculiar nauseating principle, to which the characteristic odor of the drug is due, the Pharmacopœia directs that a concentrated infusion of opium shall be treated with two successive portions of purified petroleum benzin. This plan is preferable to the more annoying treatment with ether formerly used, because no emulsion is formed and the benzin can be easily separated from the aqueous fluid. Other methods for deodorizing infusions of opium have been suggested at different times, and the following, less troublesome than the benzin treatment and equally efficacious, has been found very satisfactory by the author and many others. It was first suggested by F. T. Gordon in 1900. An infusion obtained by exhausting 100 Gm. of granulated opium with water is concentrated to 500 Cc. and heated to about 82° C. (179.6° F.); 150 Gm. of paraffin, melting at about 50° C. (122° F.), are now added in small pieces, and when liquefied the mixture is thoroughly stirred or shaken for ten minutes until the paraffin no longer seems to darken in color. After cooling the hardened crust of paraffin is broken, the deodorized liquid poured off, and the dish and under side of the paraffin washed with a little cold water, the washings being added to the decanted liquid. The mixture is filtered through paper and the filtrate made up to a volume of 800 Cc. by addition of water, after which 200 Cc. of alcohol are added, and finally enough water to bring the volume up to 1000 Cc.

Tincture of deodorized opium is of lighter color than the ordinary tincture of opium and without the disagreeable narcotic odor of the latter, but is directed to be of the same morphine strength.

Tinctura Physostigmatis; Tincture of Physostigma, also known as **Tincture of Calabar Bean.**—The present tincture is about one-third weaker than that formerly official, and should contain in each Cc. 0.00014 Gm. of the ether-soluble alkaloids of the drug. It is of a pale brownish-yellow color, and should be preserved in small, well-stoppered vials, protected from light, on account of the sensitiveness of the alkaloidal salts, when in solution, to the influence of air and light.

Tinctura Quassiæ; Tincture of Quassia.—This tincture has a light brownish-yellow color and a persistently bitter taste. It differs from most bitter tinctures in not being colored black or green by addition of ferric salts, since it contains no tannin. The present tincture is twice as strong as the former.

Tinctura Quillajæ; Tincture of Quillaja, or Soapbark.—Boiling water extracts all the saponaceous principles from quillaja, but also considerable inert matter, which is sought to be removed, in the official process for making the tincture, by addition of alcohol; the latter also finally preserves the finished product.

Tinctura Sanguinariæ; Tincture of Sanguinaria, also known as **Tincture of Bloodroot.**—The addition of acetic acid (2 per cent. by volume of the intended finished product) to the menstruum not only facilitates the extraction of the alkaloidal constituents of the drug, but also materially improves the stability of the tincture. The present official tincture of sanguinaria is only two-thirds as strong as the former.

Tinctura Stramonii; Tincture of Stramonium.—Stramonium seed having been replaced by the leaves in the Pharmacopœia, the tincture is now made from the latter. Since stramonium leaves vary somewhat in their alkaloidal content, the tincture should be made from leaves which have been assayed, in order to insure the full amount of alkaloids in the finished product, which is 0.0003 Gm. in each Cc. Tincture of stramonium has a greenish-brown color and a peculiar odor reminding somewhat of belladonna, but more pronounced.

Tinctura Strophanthi; Tincture of Strophanthus.—Since the seed of Strophanthus Kombé is the only variety officially recognized, the tincture should be made from it. When prepared strictly according to the Pharmacopœia, the tincture is at first cloudy and gradually deposits fatty matter, slowly becoming brighter. Strophanthus seeds contain considerable fixed oil, which can be removed by percolation with ether, before using the official menstruum; ether does not affect the active principle strophanthin, which is perfectly soluble in diluted alcohol. The use of ether has been objected to on account of its volatile nature and the expense, and Scoville and Loewe, in 1899, suggested the removal of the fat by a process of chilling, which has proved quite successful. The tincture prepared according to pharmacopœial directions is placed in a flask and the flask buried in a mixture of crushed ice and salt, and allowed to remain there for two hours. The temperature rapidly sinks to —14° C. (6.8° F.), and at the end of the prescribed time an abundant semi-flocculent grayish sediment will have been formed, which is removed by filtration through paper in a funnel kept packed in ice and salt. The resulting product is bright in appearance and leaves no fatty stain when evaporated on bibulous paper.

The present official tincture of strophanthus is twice as strong as the former, representing in each Cc. 0.10 Gm. of the seed.

Tinctura Vanillæ; Tincture of Vanilla.—This preparation is frequently called Extract of Vanilla, although the commercial extracts of vanilla do not by any means all correspond to the official article. Many of the commercial products are colored solutions of synthetic vanillin in alcohol and water, and, if so made, can be readily distinguished from the tincture made from the bean by the following method: Evaporate some of the extract of vanilla on a water-bath so as to get rid of the alcohol, make up the original volume by addition of water, and acidify with acetic acid; a reddish-brown precipitate of resin will form in the case of an extract made from the bean, while absence of such resin will indicate that it was a solution of vanillin or perhaps coumarin. The filtrate from such resin, in the case of the official tincture, should give a copious precipitate upon the addition of solution of basic lead acetate. In case the extract was made partly from vanilla bean and partly from synthetic vanillin, the amount of precipitate must be compared with that obtained from a like quantity of extract known to be made from bean only.

It should be borne in mind that, since tincture of vanilla is used altogether as a flavoring agent, the flavor will be much improved by age, and it is a good plan to set the finished product aside for six months or longer before using.

Tinctura Veratri; Tincture of Veratrum.—The name Tincture of Veratrum Viride having been dropped from the Pharmacopœia, it should be remembered that the official drug veratrum may indicate either the green or white variety of veratrum, or both. The present tincture has been reduced to one-fourth the strength of the former and represents in each Cc. 0.10 Gm. of veratrum, hence the dose must be increased accordingly.

Tincturæ Herbarum Recentium; Tinctures of Fresh Herbs.—These tinctures can, of course, only be made from such plants as grow in this country, and must vary in quality according to the amount of moisture present in the drug; the use of alcohol as a menstruum prevents the solution of much inert matter, and insures the presence in the finished product of all constituents soluble in a strongly alcoholic fluid.

CHAPTER XXI.

WINES AND VINEGARS.

THESE two classes of preparations are but little used by physicians at the present time, and their number has been gradually diminished. The Pharmacopœia now recognizes 10 official wines and 2 vinegars.

WINES.

Both white and red wines are recognized in the Pharmacopœia; but in the preparation of the official medicated wines, with one exception, only the white wine is directed, on account of its lesser astringency, and in 5 cases the alcoholic strength of the preparation is increased by the addition of alcohol. This fortification of the wine is particularly necessary to insure the stability of vegetable solutions during warm weather. Native wines can now be obtained of good quality, and are given preference by the Pharmacopœia. The chief difference between white and red wines lies in the dark coloring-matter and larger proportion of tannin in the latter, due to the fact that in the case of red wines the pericarp, or skin of the grape, is allowed to remain with the expressed juice during fermentation; were the skins carefully removed, many dark-colored grapes would also yield white wines, for the juice is naturally colorless. Much of the tannin found in wines may also be derived from the casks in which they are stored. As white wines, as a rule, contain only very small proportions of tannin, they are preferred as menstrua for medicated wines.

The presence of appreciable quantities of tannin in wine is decidedly objectionable if the wine is to be used in connection with iron and other metallic salts; moreover, tannin is incompatible with alkaloids, and hence wine not deprived of its tannin should never be used as a menstruum for alkaloidal drugs. The process of freeing wines from tannin is termed detannating them, and is a very simple operation. The simplest plan is to add ½ ounce of gelatin in No. 40 or No. 60 powder to 1 gallon of the wine, and agitate occasionally during twenty-four or forty-eight hours; then filter. The operation is preferably carried out during cold weather or in a cold apartment, as heat will cause the gelatin to dissolve, and the maceration must be continued until a small portion of the wine mixed with a few drops of ferric chloride solution shows no darkening of color. Gelatin in large pieces is not suitable, especially with wines containing much tannin, since the newly formed tannate of gelatin will be deposited on the surface and prevent further intimate contact of the gelatin with the wine. Formerly freshly prepared ferric hydroxide was much employed for detannating wine, but the chief objection to its use is the fact that some iron invariably is taken up by the acid present in the wine; moreover, the process is more tedious than in the case of gelatin. As the removal of tannin from wine in no way interferes with its quality—alcoholic strength and aroma remaining the same, and only coloring-matter being lost—a supply of detannated wine should be kept on hand, for it requires very little more labor to detannate a gallon than a pint.

If ferric hydroxide is to be used, it must be freshly prepared, and a convenient quantity then be added to the wine—about 8 ounces of the expressed, but moist, precipitate to a gallon.

Both white and red wines have an acid reaction, due to potassium bitartrate held in solution; this acidity is limited, by the Pharmacopœia, to from 4.49 to 7.78 Gm. of free acid per liter. The amount of solid matter in wines should range between 1.5 and 3.5 per cent., and may be ascertained by evaporation and drying on the water-bath during twelve hours. The Pharmacopœia also specifies the alcoholic strength to be from 7 to 12 per cent. by weight, which is equal to 8.5 to 15 per cent. by volume, of absolute alcohol, the official directions for ascertaining the percentage of alcohol present being to take the specific gravity of the wine at 15.6° C. (60° F.), evaporate a carefully measured portion of it, in a tared capsule, to one-third of its weight, cool and restore the original volume by the addition of water, and again take the specific gravity of the liquid at 15.6 ° C. (60° F.); the difference between the two specific gravities subtracted from 1.000 indicates the specific gravity of an alcohol containing the same percentage of absolute alcohol as the wine, the corresponding percentage being ascertained by reference to the alcoholometric tables published in the Pharmacopœia. Suppose the wine before evaporation has a specific gravity of 0.9930, and after evaporation and addition of water, 1.0098: then $1.0098 - 0.9930 = 0.0168$, and $1.000 - 0.0168 = 0.9832$; by referring to the tables it is found that alcohol of 0.9832 specific gravity at 15.6 C. (60° F.) contains between 10 and 11 per cent. by weight, or between 12 and 13 per cent. by volume, of absolute alcohol.

Red wines are frequently colored artificially with aniline, which coloration may be detected by the tests officially directed for that purpose. If red wine be mixed with twice its volume of potassa solution and a small quantity of chloroform, and the mixture then carefully heated, the presence of certain aniline colors will develop a very disagreeable odor, due to the formation of isonitril. Fuchsine may be detected by the crimson color imparted to uncolored silk fibre placed in contact with a mixture of acetic acid and an ethereal extract of red wine previously treated with ammonia-water in excess; as the mixture is evaporated in a porcelain dish the color is developed. Hydrochloric acid should not produce a red color if added to a filtrate obtained from shaking warm red wine with manganese dioxide, showing the absence of sulpho-fuchsine.

THE OFFICIAL MEDICATED WINES.—With one exception, wine of opium, these are all prepared by simple solution of the medicinal agent in the menstruum. Owing to their limited use, they should be made in small quantities only.

TABLE OF OFFICIAL WINES SHOWING STRENGTH AND MENSTRUUM USED.

Made by Maceration.

Official Names.	Quantity of drug used for 1000 Cc.	Fineness of Powder.	Menstruum.	Length of time of Maceration.
Vinum Opii; Wine of Opium	Opium 100 Gm. Cinnamon 10 " Cloves 10 "	Fine Powder No. 60 No. 30	White wine 850 Cc. Alcohol 150 "	7 days.

Although not a standardized preparation, if properly made, wine of opium is of the same morphine strength as the tincture, namely, 0.012–0.0125 Gm. in each Cc. It was formerly known as Sydenham's Laudanum.

Made by Simple Solution.

Official Name.	Composition.	
Vinum Antimonii; Wine of Antimony	Antimony and Potassium Tartrate	4 Gm.
	Boiling Distilled Water	65 Cc.
	Alcohol	175 "
	White Wine, sufficient to make	1000 "
Vinum Cocæ; Wine of Coca	Fluidextract of Coca	65 "
	Alcohol	75 "
	Sugar	65 Gm.
	Red Wine, sufficient to make	1000 Cc.
Vinum Colchici Seminis; Wine of Colchicum Seed	Fluidextract of Colchicum Seed	100 "
	Alcohol	150 "
	White Wine	750 "
Vinum Ergotæ; Wine of Ergot . . .	Fluidextract of Ergot	200 "
	Alcohol	50 "
	White Wine	750 "
Vinum Ferri: Wine of Iron. (This wine was formerly officially known as Vinum Ferri Citratis; Wine of Ferric Citrate)	Iron and Ammonium Citrate	40 Gm.
	Tincture of Sweet Orange Peel	60 Cc.
	Syrup	100 "
	White Wine, sufficient to make	1000 "
Vinum Ferri Amarum; Bitter Wine of Iron	Soluble Iron and Quinine Citrate	50 Gm.
	Tincture of Sweet Orange Peel	60 Cc.
	Syrup	300 "
	White wine, sufficient to make	1000 "
Vinum Ipecacuanhæ; Wine of Ipecac	Fluidextract of Ipecac	100 "
	Alcohol	100 "
	White Wine	800 "

VINEGARS.

The valuable solvent as well as preservative properties of diluted acetic acid were at one time employed for a larger class of preparations than at present, of which the vinegar of opium and vinegar of squill alone are now recognized in the Pharmacopœia. The official diluted acetic acid is made by mixing 1 part of 36 per cent. acetic acid with 5 parts of water, and contains, therefore, 6 per cent. of absolute acetic acid.

THE OFFICIAL VINEGARS.—These are made by maceration and subsequent expression, and represent 10 Gm. of the drug in 100 Cc. of finished product.

Acetum Opii.—Vinegar of opium is made by macerating 100 Gm. of powdered opium and 30 Gm. of nutmeg in No. 30 powder, with 500 Cc. of diluted acetic acid, for seven days, with frequent agitation; after expressing the liquid the residue is mixed with 200 Cc. of diluted acetic acid and again expressed. After mixing and filtering the liquids, 200 Gm. of sugar are dissolved in the filtrate, and sufficient diluted acetic acid is added to bring the volume up to 1000 Cc.

Vinegar of opium is of about the same morphine strength as the tincture and wine, containing 0.012–0.125 Gm. in each Cc.

Acetum Scillæ; Vinegar of Squill.—The Pharmacopœia directs that 100 Gm. of squill in coarse (No. 20) powder be macerated with 900 Cc. of diluted acetic acid during 7 days, with frequent stirring; the mixture is then strained through muslin and the dregs on the strainer washed with sufficient menstruum to bring the volume of the strained liquid nearly up to 1000 Cc. After heating this liquid to boiling, it is filtered while hot, and when cool enough diluted acetic acid is added to the filtrate to make the product measure 1000 Cc.

CHAPTER XXII.

FLUIDEXTRACTS.

THE term fluidextract, in its present acceptation, is applied to concentrated alcoholic or hydro-alcoholic solutions of vegetable principles, which are permanent and represent all the active virtues of the drugs from which they are made; they are officially recognized in the Pharmacopœias of the United States, Great Britain, Germany, and Switzerland, differing but slightly in strength in the four countries.

Fluidextracts, or liquid extracts, as they are called in Great Britain, were first introduced about the year 1832; their origin, although generally credited to American pharmacy, belongs more probably to England, since in 1834 English fluidextracts were already known in this country. Prior to 1847 very little interest appears to have been taken in this class of preparations in the United States, only 3 fluidextracts being on record as in use at that time—namely, senna, valerian, and rhubarb; from that time forward fluidextracts grew in favor, and the Pharmacopœia of 1850 gave working formulas for 7 concentrated solutions, of which, however, only 1—valerian—is deserving of the title of fluidextract in the present definition of that term; 2 were oleoresins—cubebs and black pepper; and 4 concentrated syrups—rhubarb, sarsaparilla, senna, and spigelia and senna. In 1860 the number of fluidextracts officially recognized was increased to 25, in 1870 to 46, in 1880 to 79, in 1890 to 88, and in the present (1900) edition of the Pharmacopœia 85 are directed. Besides these a large number of unofficial fluidextracts are annually produced, and this class of preparations must be considered as the most important galenicals used by physicians.

Prior to 1880 the strength of fluidextracts, as prescribed by the Pharmacopœia, was 1 grain of drug to 1 minim of fluidextract; since that time the pharmacopœial strength is based upon the relation of the metric measures of weight and capacity, so that any weight of a given drug is to be converted into a fluidextract having the bulk of the same weight of water at its maximum density, or, in other words, 1 Gm. of the drug is represented by 1 Cc. of the fluidextract. The exceptions to this rule are the fluidextracts of aconite, belladonna root, cinchona, coca, colchicum seed, conium, hydrastis, hyoscyamus, guarana, ipecac, nux vomica, pilocarpus, scopola, and stramonium, all of which are directed to be standardized to definite alkaloidal strength. British liquid extracts, with the exception of those of belladonna, cinchona, ipecac, licorice, nux vomica, male fern, opium, and pareira, are of the strength of 1 avoirdupois ounce to 1 imperial fluidounce, which practically corresponds to our own. In Germany each Gm. of drug is represented by 1 Gm. of fluidextract, the relation being weight for weight.

All the official fluidextracts are directed to be prepared by percolation, a menstruum uniform in alcoholic strength being employed during the process of exhaustion. When, however, glycerin is used with the first portion of the menstruum, percolation is continued and finished with a liquid of the same alcoholic strength, but not mixed with glycerin. By evaporating the weak percolate to a soft extract, most of the water is also expelled, and the comparatively small portion remaining with the extract will occasion but a slight change in the menstruum of the reserved portion, which, at the same time, is the best solvent for the extractive matter; finally, the addition of fresh menstruum will not change the alcoholic strength of the liquid.

It is important that the exhaustion of the drug be conducted as carefully as possible, so that the reserved portion may represent a solution of nearly the whole active virtues of the drug; with this end in view, the rate of percolation for 1000 Gm. of drug should be adjusted to about 3 drops per minute, at which rate about 10 Cc. can be collected in an hour. In the hands of a careful operator handling such quantities as are given in the pharmacopœial formulas, the official process yields very satisfactory results, and the danger arising from evaporation of the weak percolate may well be disregarded, since from 85 to 90 per cent. of the active principles are most likely contained in the reserved portion, therefore only a trifling proportion of the medicinal virtues of the drug will be subjected to heat.

The official directions for the preparation of fluid extracts are intended for the quantity of drug designated in the formulas, and must of necessity often be modified by manufacturers who operate upon hundreds of pounds at one time; fineness of powder, degree of packing, and rate of percolation must be adapted to the quantity of material in hand. Manufacturers in some cases resort to repeated maceration and expression instead of percolation.

Authority is given by the Pharmacopœia to employ, where it may be applicable, the process of repercolation without change of initial menstruum. This process, which is fully described on page 143, is followed by several manufacturers, and does away with the possibility of injury from application of heat. Repercolation is particularly adapted to the preparation of fluidextracts, and the only objection that can be urged against its use is the enforced necessity of carrying on hand a series of bottles containing weak percolates for each fluid extract made; disregarding this annoying feature, the process is less troublesome than any other, and in the case of some drugs must yield fluidextracts of superior quality.

All fluidextracts, no matter how carefully made, will begin to deposit soon after they are completed, and this precipitation will continue for a varying length of time. The menstruum dissolves certain extractive principles which it is incapable of retaining in perfect solution afterward under changes of temperature, and thus far no method is known to prevent entirely such separation, which is augmented by exposure to light, air, and heat. Fluidextracts prepared without heat are less prone to deposit than when made by the official process, and in these the amount of precipitate is often very trifling; happily, frequent examinations of precipitates in fluidextracts have disclosed the fact that they consist chiefly of inert extractive matter, and therefore do not affect the medicinal value of the preparation. All freshly made fluidextracts should be set aside in well-stoppered glass vessels, in dark and moderately cool places, for a period of two or three months, before filtering and bottling them; this plan is universally followed by large manufacturers, and explains the absence, in many cases, of appreciable deposits. Pharmacists will find that fluidextracts can be made from selected drugs on a small scale as perfectly as in large quantities, and simple appearance, so often misleading, is no criterion as to quality.

With few exceptions the fluidextracts of the Pharmacopœia are prepared by the following general formula; the quantity of menstruum for moistening the drug, the degree of pressure to be used in packing, and the quantity of percolate to be set aside as reserve being specified in each case:

1000 *Gm. of the powdered drug of the prescribed degree of fineness are thoroughly moistened with a certain quantity of the initial menstruum and packed more or less firmly in a cylindrical percolator; the drug having been properly covered with a paper diaphragm, enough menstruum is poured on to saturate completely the powder and leave a stratum above it. When liquid begins to drop from the percolator, close the lower orifice, and having closely covered the percolator to prevent evaporation, macerate for forty-eight hours. Then allow percolation to proceed slowly, gradually adding menstruum (alcohol or alcohol and water) until the drug is exhausted. Reserve the first* 700 *to* 900 Cc. *of the percolate, and evaporate the remainder, at a temperature not exceeding* 50° *C.* (122° *F.*), *to a soft extract; dissolve this in the reserved portion and add enough menstruum to make the fluidextract measure* 1000 *Cc.*

In the case of fluidextracts to be standardized, the Pharmacopœia does not direct the finished product to be brought up to the volume of 1000 Cc. After dissolving the soft extract, obtained by evaporation of the weak percolate, in the reserved portion, the whole is thoroughly mixed and the liquid then assayed; from the results thus obtained, the amount of active principle present in the remainder of the liquid is calculated, and sufficient menstruum is added to bring the fluidextract up to the prescribed standard.

Concentration of the weak percolate is usually effected by distilling off the alcohol in a suitable apparatus on a water-bath, and finally evaporating the liquid, in a porcelain capsule, to the proper consistence, preferably with constant stirring. The Pharmacopœia does not in every case specify the temperature for evaporation, but it is best to keep it always below 50° C. (122° F.), so as to avoid changes in the extractive as far as possible.

Arranged according to the menstruum, the official fluidextracts may be divided into 21 classes, as follows:

Made with alcohol: aromatic powder, capsicum, cimicifuga, cubeb, gelsemium, ginger, Indian cannabis, lupulin, savin, veratrum.

Made with alcohol 4 volumes, water 1 volume: belladonna root, eriodictyon, euonymus, mezereum, podophyllum, rhubarb, scopola, serpentaria, stavesacre.

Made with alcohol 3 volumes, water 1 volume: aconite, buchu, calamus, eucalyptus, grindelia, ipecac, leptandra, matico, nux vomica (with acetic acid), sumbul, valerian, xanthoxylum.

Made with alcohol 7 volumes, water 3 volumes: calumba.

Made with alcohol 2 volumes, water 1 volume: bitter orange peel, colchicum seed, hyoscyamus, stramonium, viburnum opulus, viburnum prunifolium.

Made with alcohol 6½ volumes, water 3½ volumes: convallaria.

Made with alcohol 1 volume, water 1 volume (diluted alcohol): berberis, chimaphila, chirata, coca, conium (with acetic acid), cypripedium, digitalis, ergot (with acetic acid), eupatorium, gentian, guarana, krameria, lappa, phytolacca, pilocarpus, quillaja, rubus, scutellaria, senna, spigelia, stillingia, taraxacum.

Made with alcohol 5 volumes, water 8 volumes: frangula.

Made with alcohol 4 volumes, water 6 volumes: cascara sagrada.

Made with alcohol 1 volume, water 2 volumes: quassia, sarsaparilla.

Made with alcohol 8 volumes, glycerin 1 volume, water 1 volume, followed by a mixture of alcohol 8 volumes, water 2 volumes: cinchona.

Made with alcohol 6 volumes, water 3 volumes, glycerin 1 volume, followed by a mixture of alcohol 2 volumes, water 1 volume: hydrastis.

Made with alcohol 6 volumes, water 3 volumes, glycerin 1 volume, followed by a mixture of alcohol 6 volumes, water 4 volumes: apocynum, geranium, pareira.

Made with diluted alcohol 9 volumes, glycerin 1 volume, followed by diluted alcohol: pomegranate, quercus, rhus glabra, rose, sarsaparilla (compound fluidextract).

Made with alcohol 3 volumes, water 6 volumes, glycerin 1 volume, followed by a mixture of alcohol 1 volume, water 2 volumes: hamamelis.

Made with alcohol 2 volumes, water 5 volumes, glycerin 3 volumes: uva ursi.

Made with alcohol 2 volumes, water 6 volumes, glycerin 2 volumes: wild cherry.

Made with alcohol 6 volumes, water 3 volumes, solution of potassium hydroxide 0.3 volume: senega.

Made with alcohol 2 volumes, glycerin 1 volume, water 1 volume, followed by diluted alcohol: aromatic cascara sagrada.

Made with diluted acetic acid, 10 per cent. solution: lobelia, sanguinaria, squill.

Made with boiling water, glycyrrhiza, triticum. Finished product contains about 25 per cent. by volume of alcohol as a preservative, and in the case of glycyrrhiza also 25 per cent. of glycerin and 5 per cent. of ammonia water.

ALPHABETICAL LIST OF OFFICIAL FLUIDEXTRACTS.

Showing the fineness of powder, menstruum, degree of moisture, and reserve percolate directed by the Pharmacopœia.

Name.	Fineness of Powder.	Initial Menstruum.	Quantity of Menstruum to moisten 1000 Gm. of the drug.	Reserve.
Fluidextract of—				
Aconite	No. 60	Alcohol 750 Cc. Water 250 "	400 Cc.	800 Cc.
Apocynum	" 60	Alcohol 600 " Glycerin 100 " Water 300 "	400 "	900 "
Aromatic Powder	. . .	Alcohol	350 "	850 "
Belladonna Root	" 60	Alcohol 800 " Water 200 "	350 "	800 "
Berberis	" 60	Diluted Alcohol	400 "	700 "
Bitter Orange Peel	" 40	Alcohol 600 " Water 300 "	350 "	800 "
Buchu	" 60	Alcohol 750 " Water 250 "	400 "	850 "
Calamus	" 40	Alcohol 750 " Water 250 "	350 "	900 "
Calumba	" 20	Alcohol 700 " Water 300 "	300 "	700 "
Cannabis Indica	" 30	Alcohol	300 "	900 "
Capsicum	" 50	Alcohol	500 "	900 "
Cascara Sagrada	" 40	Alcohol 400 " Water 600 "	400 "	800 "
Cascara Sagrada (Aromatic)	" 40	Alcohol 500 " Glycerin 250 " Water 250 "	400 "	800 "
Chimaphila	" 30	Diluted Alcohol	400 "	800 "
Chirata	" 30	Diluted Alcohol	350 "	850 "
Cimicifuga	" 60	Alcohol	250 "	900 "
Cinchona	" 60	Alcohol 800 " Glycerin 100 " Water 100 " followed by Alcohol 800 " Water 200 "	350 "	700 "
Coca	" 40	Diluted Alcohol	450 "	700 "
Colchicum Seed	" 50	Alcohol 600 " Water 300 "	300 "	750 "
Conium	" 40	Diluted Alcohol 980 " Acetic Acid 20 "	300 "	800 "
Convallaria	" 60	Alcohol 650 " Water 350 "	400 "	800 "
Cubeb	" 40	Alcohol	200 "	900 "
Cypripedium	" 60	Diluted Alcohol	350 "	850 "
Digitalis	" 60	Diluted Alcohol	400 "	850 "
Ergot	" 60	Diluted Alcohol 980 " Acetic Acid 20 "	300 "	850 "
Eriodictyon	" 60	Alcohol 800 " Water 200 "	400 "	900 "

ALPHABETICAL LIST OF OFFICIAL FLUIDEXTRACTS.—*Continued.*

Name.	Fineness of Powder.	Initial Menstruum.	Quantity of Menstruum to moisten 1000 Gm. of the drug.	Reserve.
Fluidextract of—				
Eucalyptus	No. 40	Alcohol 750 Cc. Water 250 "	400 Cc.	900 Cc.
Euonymus	" 40	Alcohol 800 " Water 200 "	350 "	800 "
Eupatorium	" 40	Diluted Alcohol	400 "	800 "
Frangula	" 40	Alcohol 500 " Water 800 "	350 "	800 "
Gelsemium	" 60	Alcohol	300 "	900 "
Gentian	" 30	Diluted Alcohol	350 "	800 "
Geranium	" 30	Alcohol 600 " Glycerin 100 " Water 300 "	350 "	800 "
Ginger	" 50	Alcohol	250 "	900 "
Glycyrrhiza	" 20	Boiling Water	400 "	
Grindelia	" 30	Alcohol 750 " Water 250 "	300 "	850 "
Guarana	" 60	Diluted Alcohol	200 "	700 "
Hamamelis Leaves .	" 40	Alcohol 300 " Glycerin 100 " Water 600 "	350 "	850 "
Hydrastis	" 60	Alcohol 600 " Glycerin 100 " Water 300 "	300 "	750 "
Hyoscyamus	" 60	Alcohol 600 " Water 300 "	400 "	800 "
Ipecac	" 80	Alcohol 750 " Water 250 "	350 "	850 "
Krameria	" 40	Diluted Alcohol	400 "	800 "
Lappa	" 60	Diluted Alcohol	400 "	800 "
Leptandra	" 60	Alcohol 750 " Water 250 "	400 "	850 "
Lobelia	" 50	Acetic Acid (36 per cent.) 275 " Water 725 "	350 "	900 "
Lupulin	. . .	Alcohol		900 "
Matico	" 40	Alcohol 750 " Water 250 "	300 "	850 "
Mezereum	" 30	Alcohol 800 " Water 200 "	400 "	900 "
Nux Vomica	" 60	Alcohol 750 " Water 250 " Acetic Acid 50 "	1000 "	900 "
Pareira	" 40	Alcohol 600 " Glycerin 100 " Water 300 "	400 "	850 "
Phytolacca	" 40	Diluted Alcohol	400 "	800 "
Pilocarpus	" 40	Diluted Alcohol	350 "	750 "
Podophyllum	" 40	Alcohol 800 " Water 200 "	300 "	850 "
Pomegranate	" 30	Diluted Alcohol 900 " Glycerin 100 " followed by Diluted Alcohol	400 "	800 "
Quassia	" 40	Alcohol 300 " Water 600 "	400 "	900 "
Quercus	" 40	Diluted Alcohol 900 " Glycerin 100 " followed by Diluted Alcohol	400 "	700 "
Quillaja	" 40	Diluted Alcohol	400 "	800 "
Rhubarb	" 30	Alcohol 800 " Water 200 "	400 "	750 "
Rhus Glabra	" 40	Diluted Alcohol 900 " Glycerin 100 "	350 "	800 "
Rose	" 20	Diluted Alcohol 900 " Glycerin 100 "	400 "	750 "
Rubus	" 40	Diluted Alcohol	350 "	800 "
Sanguinaria	" 30	Acetic Acid (36 per cent.) 275 " Water 725 "	300 "	850 "
Sarsaparilla	" 30	Alcohol 300 " Water 600 "	400 "	800 "

ALPHABETICAL LIST OF OFFICIAL FLUIDEXTRACTS.—*Continued.*

Name.	Fineness of Powder.	Initial Menstruum.	Quantity of Menstruum to moisten 1000 Gm. of the drug.	Reserve.
Fluidextract of—				
Sarsaparilla, Compound	No. 30	Diluted Alcohol 900 Cc. Glycerin 100 " followed by Diluted Alcohol	400 Cc.	800 Cc.
Savin	" 40	Alcohol	250 "	900 "
Scopola	" 40	Alcohol 800 " Water 200 "	350 "	800 "
Scutellaria	" 40	Diluted Alcohol	350 "	800 "
Senega	" 40	Alcohol 600 " Water 300 " Potassium Hydroxide Solution 30 "	450 "	850 "
Senna	" 40	Diluted Alcohol, after extraction with alcohol and rejection of the latter.	400 "	800 "
Serpentaria	" 50	Alcohol 800 " Water 200 "	300 "	900 "
Spigelia	" 40	Diluted Alcohol	300 "	850 "
Squill	" 20	Acetic Acid (36 per cent.) 275 " Water 725 "	800 "	
Stavesacre	" 40	Alcohol 800 " Water 200 "	300 "	800 "
Stillingia	" 40	Diluted Alcohol	300 "	850 "
Stramonium	" 40	Alcohol 600 " Water 300 "	400 "	800 "
Sumbul	" 30	Alcohol 750 " Water 250 "	400 "	850 "
Taraxacum	" 30	Diluted Alcohol	300 "	800 "
Triticum	Finely cut	Boiling Water		
Uva Ursi	No. 30	Alcohol 200 " Glycerin 300 " Water 500 "	400 "	800 "
Valerian	" 40	Alcohol 750 " Water 250 "	300 "	850 "
Veratrum	" 60	Alcohol	300 "	900 "
Viburnum Opulus	" 40	Alcohol 600 " Water 300 "	300 "	850 "
Viburnum Prunifolium	" 40	Alcohol 600 " Water 300 "	300 "	850 "
Wild Cherry	" 30	Alcohol 200 " Glycerin 200 " Water 600 "	300 "	
Xanthoxylum	" 40	Alcohol 750 " Water 250 "	250 "	900 "

SPECIAL REMARKS.

Fluidextractum Aconiti; Fluidextract of Aconite.—The standard fixed by the Pharmacopœia for this fluidextract is 0.004 Gm. of aconitine in each Cc., to be determined by titration with volumetric acid solution.

Fluidextractum Belladonnæ Radicis; Fluidextract of Belladonna Root.—As indicated in the title, this preparation must always be made from the root of belladonna. The standard fixed by the Pharmacopœia is 0.005 Gm. of mydriatic alkaloids in each Cc., to be determined by titration with volumetric acid solution. The liquid extract of the British Pharmacopœia, also made from root, is 50 per cent. stronger, containing 0.0075 Gm. of alkaloids in each Cc.

Fluidextractum Cannabis Indicæ; Fluidextract of Indian Cannabis, also called **Fluidextract of Indian Hemp.**—There seems to be little need for this preparation in the Pharmacopœia, since an extract and a tincture of Indian hemp are official. Much of the commercial drug is of poor quality, and it seems desirable to have the fluidextract tested physiologically before it is used. Fluidextract of Indian hemp seems particularly suited for the process of repercolation, since the constituents of the drug are easily affected by heating with exposure to air.

Fluidextractum Cinchonæ; Fluidextract of Cinchona, also sometimes called **Fluidextract of Calisaya Bark.**—The standard fixed by the Pharmacopœia for this fluidextract is 0.04 Gm. of anhydrous ether-soluble alkaloids in each Cc., to be determined gravimetrically, after the alkaloids have been dried for ½ hour at a temperature of 120° C. (248° F.). The British liquid extract of cinchona is made from red cinchona and contains 0.05 Gm. of alkaloids in each Cc.

Fluidextractum Cocæ; Fluidextract of Coca.—The standard fixed by the Pharmacopœia for this fluidextract is 0.005 Gm. of ether-soluble alkaloids, to be determined by titration with volumetric acid solution.

Fluidextractum Colchici Seminis; Fluidextract of Colchicum Seed.—The standard fixed by the Pharmacopœia for this fluidextract is 0.005 Gm. of colchicine in each Cc., to be determined gravimetrically.

Fluidextractum Conii; Fluidextract of Conium.—The standard fixed for this fluidextract is 0.0045 Gm. of coniine in each Cc. Since the alkaloid coniine is volatile, it is better to convert it into its hydrochloride and to weigh it in that form. The weight of coniine hydrochloride obtained, if multiplied by 0.777, will represent the weight of absolute coniine. The use of acetic acid in the menstruum is for the purpose of facilitating the extraction of the alkaloid and to prevent its loss during evaporation.

Fluidextractum Glycyrrhizæ; Fluidextract of Glycyrrhiza, also known as **Fluidextract of Licorice.**—The directions to exhaust licorice root solely with boiling water are based upon the experience that a less acrid preparation is obtained. Since the root swells considerably when treated with hot water, the Pharmacopœia very properly directs loose packing in the percolator. After concentration of the percolate to less than ½ the volume of the intended finished product, it is mixed with an equal volume of alcohol for the purpose of removing mucilaginous matter, and filtered after 3 days. The bulk of the alcohol is recovered from the filtrate by distillation; glycerin, ammonia-water, and alcohol are added, and finally sufficient water to bring the finished product up to the prescribed volume. The fluidextract contains 25 per cent. by volume of glycerin, 20 per cent. of alcohol, and 5 per cent. of ammonia-water.

Fluidextractum Guaranæ; Fluidextract of Guarana.—The standard fixed by the Pharmacopœia for this fluidextract is 0.035 Gm. of the alkaloids from guarana, chiefly caffeine, to be determined gravimetrically after drying the alkaloidal residue to constant weight on a water-bath.

Fluidextractum Hydrastis; Fluidextract of Hydrastis, also known as **Fluidextract of Golden Seal.**—The standard fixed by the Pharmacopœia for this fluidextract is 0.02 Gm. of hydrastine, the white alkaloid of the drug, in each Cc., to be determined gravimetrically, after having dried the alkaloid to constant weight on a water-bath.

Fluidextractum Hyoscyami; Fluidextract of Hyoscyamus, also known as **Fluidextract of Henbane.**—The standard fixed for this fluidextract by the Pharmacopœia is 0.00075 Gm. of the alkaloids from hyoscyamus in each Cc., to be determined by titration with volumetric acid solution.

Fluidextractum Ipecacuanhæ; Fluidextract of Ipecac.—The standard fixed by the Pharmacopœia for this fluidextract is 0.0175 Gm. of the mixed alkaloids from ipecac root in each Cc., to be determined by titration with volumetric acid solution. The liquid extract of ipecac of the British Pharmacopœia is stronger than our own, containing from 0.02 to 0.0225 Gm. of alkaloids in each Cc.

Fluidextractum Lobeliæ; Fluidextract of Lobelia.—This is one of the new class of fluidextracts, prepared with 10 per cent. acetic acid as a menstruum, and contains no alcohol. It has been found by experiments that certain drugs are well suited for this treatment, and that the finished product keeps as well as if made with alcoholic or hydro-alcoholic menstrua, represents the full virtues of the drug, and is less liable to precipitation when mixed with aqueous liquids. The fluidextracts of sanguinaria and squill are made in the same manner as fluidextract of lobelia.

The name acetracts has been proposed as a distinctive title for this class of fluidextracts, but it is very doubtful whether it will ever be officially adopted.

Fluidextractum Nucis Vomicæ; Fluidextract of Nux Vomica.—The standard fixed by the Pharmacopœia for this fluidextract is different from that heretofore prescribed, being 0.01 Gm. of strychnine in each Cc., to be determined by titration with volumetric acid solution. The proportion of strychnine in the total alkaloids of nux vomica varying from 45 to 55 per cent., the present fluidextract is about one-third stronger than heretofore. As powdered extract of nux vomica contains 5 per cent. of strychnine, small quantities of the fluidextract may be made by dissolving 2 Gm. of the powdered extract in sufficient menstruum (alcohol 3 volumes, water 1 volume) to make 10 Cc. of solution. The British liquid extract of nux vomica is 50 per cent. stronger than our own, containing 0.015 Gm. of strychnine in each Cc.

Fluidextractum Pilocarpi; Fluidextract of Pilocarpus, also known as **Fluidextract of Jaborandi.**—The standard fixed by the

Pharmacopœia for this fluidextract is 0.004 Gm. of the alkaloids from pilocarpus in each Cc., to be determined by titration with volumetric acid solution.

Fluidextractum Quercus; Fluidextract of Quercus, also known as **Fluidextract of Oak Bark.**—Since only white-oak bark is officially recognized under the title Quercus, the commercial fluidextract of red-oak bark should not be used when simply fluidextract of quercus is prescribed.

Fluidextractum Quillajæ; Fluidextract of Quillaja, also known as **Fluidextract of Soapbark.**—On account of the toxic properties of soap-bark, the use of the fluidextract in medicine is extremely limited, and the value of the preparation in pharmacy is very questionable.

Fluidextractum Rhamni Purshianæ Aromaticum; Aromatic Fluidextract of Cascara Sagrada.—This preparation is sometimes called Aromatic Cascara, and is also known as Tasteless Fluidextract of Cascara, although it is not by any means tasteless. The magnesia is used for the purpose of destroying the very bitter taste of the cascara bark, and the addition of licorice root and compound spirit of orange materially improves the taste of the finished product. It has been stated that maceration with water and subsequent drying before moistening with menstruum are not essential for the complete destruction of the bitter taste, but in the author's experience this modification of the process is not satisfactory. Slaked lime has also been suggested in place of magnesia, but has been found inefficient and yields an inferior preparation. The finished product, if carefully made, has a pleasant, sweetish taste.

Fluidextractum Rubi; Fluidextract of Rubus, also known as **Fluidextract of Blackberry Root.**—The menstruum heretofore used for this fluidextract did not yield an entirely satisfactory preparation, and it was thought that perhaps an increase in the proportion of glycerin might overcome the difficulty, but, according to Prof. Remington, the best results are obtained by omitting all glycerin and using diluted alcohol alone.

Fluidextractum Scopolæ; Fluidextract of Scopola.—This preparation so closely resembles fluidextract of belladonna root in constituents and medicinal value that it is practically identical with the same. The standard fixed by the Pharmacopœia is also 0.005 Gm. of mydriatic alkaloids in each Cc., to be determined by titration with volumetric acid solution.

Fluidextractum Senegæ; Fluidextract of Senega.—The addition of potassium hydroxide solution to the menstruum is for the purpose of forming soluble compounds with the pectin principles present in the root, and thus prevent gelatinization of the fluidextract. Ammonia-water was employed formerly for the same purpose, but a solution of the fixed alkalies seems preferable.

Fluidextractum Sennæ; Fluidextract of Senna.—The present fluidextract is a quite different preparation from that formerly official, inasmuch as the drug is first treated by percolation with strong alcohol, whereby odorous resinous matter is removed, to which the griping effect of senna is due. The alcoholic tincture is rejected, and the senna, having been dried, is then extracted with diluted alcohol and the fluidextract made according to the general formula. The finished product represents all the valuable medicinal virtues of the drug.

Fluidextractum Stillingiæ; Fluidextract of Stillingia.—This fluidextract will sometimes gelatinize on standing; this may be avoided by using a stronger alcoholic menstruum (alcohol 3 volumes, water 1 volume), or by adding sugar in the proportion of 10 to 12 per cent. of the weight of the drug.

Fluidextractum Stramonii; Fluidextract of Stramonium.—The official title now refers to the fluidextract of stramonium leaves, since stramonium seed is no longer recognized. The standard fixed by the Pharmacopœia for this fluidextract is 0.0035 Gm. of mydriatic alkaloids in each Cc., to be determined by titration with volumetric acid solution.

Fluidextractum Taraxaci; Fluidextract of Taraxacum, also known as **Fluidextract of Dandelion Root.**—The addition of sodium hydroxide solution to the concentrated tincture is for the purpose of neutralizing the acidity present and thus produce a preparation miscible with alkali carbonates or bicarbonates without effervescence.

Fluidextractum Tritici; Fluidextract of Triticum, also known as **Fluidextract of Couch Grass.**—Although the Pharmacopœia directs percolation with boiling water to exhaustion, digestion of the finely cut drug will be found equally useful in every way, the operation to be repeated once or twice, as may be necessary; the infusion should then be rapidly concentrated, and when cold mixed with the alcohol and set aside for 48 hours, whereby mucilaginous and albuminous matter is separated. The finished product contains 25 per cent. of alcohol, which protects the saccharine liquid against fermentation.

Fluidextractum Veratri; Fluidextract of Veratrum.—Since the official title Veratrum is now understood to apply to the dried rhizome and roots of both *veratrum viride* and *veratrum album*, the name of the fluidextract has been changed accordingly.

CHAPTER XXIII.

EXTRACTS.

EXTRACTS are permanent, soft, solid, or dry preparations, obtained by evaporation of a solution of the medicinal principles of drugs. These solutions are prepared, as a rule, in the manner already explained under Fluidextracts, the solvents or menstrua employed being either water, water and alcohol, alcohol, or ether. According to the different menstrua used in their manufacture, extracts are divided into *aqueous*, *hydro-alcoholic*, *alcoholic*, and *ethereal*, the last-named class being recognized in the Pharmacopœia under the name of *oleoresins*. In fresh plants the solution of the medicinal principles is represented by the juice, and may be obtained by expression; extracts prepared by simple evaporation of the fresh juice of a plant are usually known as inspissated juices.

The U. S. Pharmacopœia does not recognize inspissated juices, since the narcotic herbs which are extensively used in Europe for this purpose are not indigenous in the United States. The juice is obtained from the fresh plant, after removal of extraneous matter, by bruising in a stone mortar with the aid of a hard-wood pestle until reduced to a smooth, pulpy mass, which is then strongly expressed in canvas bags; in order to recover all the juice, the residue is often mixed with water and again expressed. When the plant is not sufficiently moist to enable the formation of a soft pulp, water is sprinkled over it from time to time.

Besides the medicinal principles, the expressed juices of fresh herbs contain also mucilaginous and albuminous matter in solution and variable quantities of chlorophyl or green coloring-matter in suspension; of these, the albuminous principles are most objectionable, as upon concentration of the juice they undergo change and are likely to render the finished extract tough and insoluble. When roots are expressed, as in the case of the corm of colchicum, starch, which is present in the juice in place of chlorophyl, passes through the press-cloth, and must be removed by subsidence and decantation. The British, German, and French Pharmacopœias direct the removal of albuminous matter by heating the juice to from 80° to 90° C. (176° to 194° F.) and filtering. The coagulated albumen envelops the green coloring-matter and removes it also, which fact is disregarded in Germany and France, and accounts for the brown color of the extracts made from fresh herbs in those countries. In Great Britain the chlorophyl is carefully separated by heating the fresh juice to 55° C. (131° F.) and straining through calico; the liquid is then heated to 94° C. (201.2° F.), and after filtering out the coagulated albumen evaporated to a thin syrup, the chlorophyl is reincorporated and evaporation continued, with constant stirring, to the proper consistence. This explains the firm condition and fine green color of some of the British narcotic extracts. The German Pharmacopœia alone provides for the removal of the gummy matter, and hence its narcotic extracts are relatively much stronger than those of the British and French Pharmacopœias. The solubility of gummy matter is not in any way affected by heating, and therefore the filtered liquid, after removal of the coagulated albumen and chlorophyl, is evaporated to 10 per cent. of the original weight of the fresh herb used, mixed with an equal volume of alcohol, and set aside for twenty-four hours to allow the precipitated gum to subside. After decantation the precipitate is washed with diluted alcohol, which is added to the other clear liquid, and the whole evaporated to the condition of a soft solid.

Consistence of Extracts.—The U. S. Pharmacopœia recognizes three kinds of solid extracts, those of a soft, semiliquid consistence, like thick honey, those of pilular consistence, and those evaporated to complete dryness. A pilular consistence is such a condition as will allow the extract to be rolled into masses of pilular form without adhering to the fingers or subsequently losing shape; this is rarely met with in the market, except in the case of British narcotic extracts, which derive their firmness chiefly from the chlorophyl and gummy matter present. Pilular consistence for the extracts made in this country, by the official formulas, is practically unattainable at all seasons, for extracts made in summer are likely to become too hard in winter, while those evaporated to the proper consistence in winter are prone to soften in summer. Some extracts become tough and hard in the course of time; these are best retained in proper condition by incorporating with them, while still warm, 10 per cent. of their weight of glycerin, as suggested in the Pharmacopœia. The condition of complete dryness is not applicable to all extracts, but can be readily maintained for all those so directed by the Pharmacopœia, provided heat and moisture be excluded.

Of late years powdered extracts have come extensively into demand, and their convenience in dispensing pharmacy cannot be denied. Sugar of milk is to be preferred, wherever possible, as a diluent on account of its perfect solubility, but in some cases finely powdered licorice root has been found much better for maintaining the pulverulent condition of the extract, especially during damp or warm weather. The respective finely powdered drugs have also been used with success as diluents. Large manufacturers, as a rule, now prepare powdered extracts by evaporating the percolate to dryness in vacuum stills, where concentration and desiccation can be effected at a low temperature without possible injury to the constituents in solution; the dry extract is subsequently reduced to fine powder in pebble-mills, whereby heat is avoided. Powdered extracts may readily be prepared of definite strength, especially those which owe their medicinal value to alkaloidal or resinous constituents; and in the absence of specific constituents to be used as a basis for standardization, the Pharmacopœia has directed that they shall bear a definite relation to the crude drugs from which they have been respectively made. The following are the standardized extracts of the U. S. Pharmacopœia: Of definite alkaloidal strength, belladonna leaves, colchicum corm, hyoscyamus, nux vomica, opium, physostigma, scopola, and stramonium—8; representing 4 times their weight of the respective crude drugs, cascara sagrada, cimicifuga, euonymus, and leptandra—4; representing 8 times its weight of crude drug, ergot—1; representing 10 times its weight of crude drug, quassia—1. In Germany, powdered narcotic extracts are prepared of one-half the original strength of the extract, by addition of finely powdered licorice root.

The Abstracts of the U. S. Pharmacopœia for 1880 were closely allied to the present powdered extracts. They were much weaker preparations, being made to represent twice their weight of crude drug. The general plan for preparing abstracts was to make a fluidextract of the drug with strong alcohol, to mix this with some sugar of milk, dry by spontaneous evaporation in a warm place, then add sufficient sugar of milk to bring the product up to one-half the weight of the powdered drug used, and finally reduce to a fine powder.

To avoid the tendency of powdered extracts to cake, caused by their hygroscopic nature, Dr. A. B. Lyons, in 1899, introduced a line of extracts in the form of scales, for which it is claimed that they are in many respects superior to powdered extracts. These scale extracts are obtained, according to the statement of Dr. Lyons, by first preparing a highly concentrated liquid extract of the respective drugs by the use of menstrua which leave behind as much inert constituents as possible. Having ascertained by experiment how much dry residue is obtainable from these liquid extracts, sufficient acacia is added to insure a definite standard of strength, which has previously been fixed upon, in the finished product. The solution is then spread on plates of glass and dried in a current of warm air. The particular menstrua used for the different drugs have thus far not been made known. Scale extracts somewhat resemble the iron scale salts in appearance, and with warm water readily form more or less turbid solutions. As in the case of powdered extracts, those owing their value to alkaloids are brought to a definite standard of alkaloidal percentage; but in the case of other scale extracts a uniform strength has been adopted corresponding to four times the weight of the drug represented.

Changes by Evaporation.—All plants contain one or more principles, which, though originally colorless, are very easily altered under the influence of air and heat, acquiring a yellow or brown color. It is not known whether the so-called *colorless extractive* is alike in all plants, neither is its composition or the nature of the changes produced under the conditions mentioned known, except that the heat of boiling water and the prolonged action of oxygen will convert it ultimately into a blackish insoluble substance, to which the name *apotheme* has been given, and which appears to be allied to *humin*. Extractive is almost insoluble in absolute alcohol and ether, but dissolves freely in weaker alcohol and water, and is removed from its solution by animal charcoal and aluminum hydroxide, the more readily after it has become colored by oxidation. It is with difficulty freed from admixtures, and the terms sweet, bitter, acrid, etc., as applied to extractives, refer to the same body in a more or less altered condition, combined or intimately mixed with other principles to which the peculiar taste is due. The injurious influence of air and heat upon the vegetable juices is mainly confined to the alterations of this extractive, and extends, in a limited degree only, to the majority of the well-defined principles. Its effects have often been much overrated, except as regards the appearance of the extracts. The color of the different extracts varies with the nature of the drug from which they have been made, but should never be black. The characteristic taste, and to some extent also the odor of the drug, should be perceived in its extract, and it should yield a nearly clear or moderately turbid solution with the menstruum used in its preparation.

Aqueous Extracts.—While decoction in some cases increases the yield of extract, by bringing into solution starch and other inert matter, it more frequently injures the quality of the product by inducing changes in certain principles which do not occur by infusion at lower temperatures. There is but one instance, that of extract of logwood, in which the Pharmacopœia directs extraction by boiling, and this is on account of the difficulty of exhausting the tough wood. In Europe, digestion is still preferred for a few aqueous extracts, but, as a rule, maceration and percolation with cold water have been found to yield superior extracts. For the better extraction of the active virtues of the drug, an addition of acid or alkali is sometimes made, as in the case of the official extract of colchicum corm and pure extract of glycyrrhiza. In the preparation of aqueous extracts the solution is freed from objectionable matter, whenever necessary, by heating to the boiling-point and straining before final evaporation.

In 1889, the plan of concentrating large volumes of aqueous solutions of extracts by means of cold was formulated by M. Adrian, a French pharmacist, and put into practice on a large scale. Following the suggestions of Herrera (1877), M. Adrian subjects the filtered aqueous solutions to a temperature of —20° C. (—4° F.), in an ammonia ice-apparatus, and thus obtains large blocks of ice, in which the extractive solution is enveloped, the pure water alone freezing; these blocks of ice are rapidly converted into snow by means of large shaving machines. Another French pharmacist, M. Vee, prefers to convert the aqueous solution into a crystalline magma instead of solid blocks of ice, and accomplishes this by keeping the liquid in constant agitation during the freezing process. The snow-like mass is placed in centrifugal extractors, where about 75 per cent. of water is removed. The remaining solution is again subjected to cold (even a lower temperature than at first), when a syrupy liquid is obtained, which can readily be evaporated to a solid extract, in a vacuum apparatus, at a temperature not exceeding 30° C. (86° F.). Extracts thus prepared are lighter in color than those obtained by ordinary vacuum or open-air evaporation, form almost clear solutions with water, and possess the odor and taste of the drug in a marked degree. It has been found that all vegetable matter in solution is retained in its original condition, even the albumen, water alone being removed.

Alcoholic and Hydro-alcoholic Extracts.—For these two classes of extracts percolation is decidedly the best method of extracting the medicinal principles of the drugs, the operation being continued to complete exhaustion. If percolation be conducted at the rate of 5 drops per minute, from 3 to 4 Cc. of percolate should suffice for each Gm. of drug. In many cases, particularly those of the mydriatic drugs, whose active principles are easily split up by prolonged application of heat, it is very desirable to set aside the first third of the percolate as reserve, to be incorporated with the remainder when this has been reduced to the condition of a syrupy fluid. The recovery of the alcohol is effected, as in the case of fluid extracts, by distillation in a suitable still, the final evaporation being conducted in porcelain dishes, with constant stirring, so as to insure a homogeneous mass and prevent the separation of resinous and other matter. As the concentration of the solution approaches the condition of a thick syrup, continuous stirring is also necessary, to prevent the formation of a film, which, becoming gradually thicker, retards the evaporation of moisture, and consequently causes an accumulation of heat within the mass, to the possible injury of some of the constituents. In large manufacturing establishments mechanical stirrers are conveniently operated by steam, electric, or water motors. Metallic stirrers should never be employed, only those of porcelain, glass, or wood being permissible. To guard against the separation of coloring-matter or changes in other constituents of the solution, concentration should always be effected on a water-bath, at a temperature not exceeding 50° C. (122° F.).

Very closely allied to extracts are two preparations which, although not partaking of the character of concentrated solutions, yet resemble some of the finished extracts in their physical properties; they are purified aloes and purified ox-gall.

Aloe Purificata; Purified Aloes.—The official directions for purifying aloes are to melt 1000 Gm. of aloes by means of a water-bath, and, after addition of 200 Cc. of alcohol, to stir the mixture well and pass it through a No. 60 sieve which has been dipped into boiling water. The strained mixture is evaporated on a water-bath until a thread of the mass, upon cooling, becomes brittle; it may then be preserved in lumps of convenient size in a cool, dry place.

The process is strictly one of mechanical purification, the object being the removal of pieces of wood, leaves, and other foreign matter usually found in aloes; the alcohol is added simply to thin down the melted aloes and facilitate straining. By dipping the sieve into boiling water, chilling and adhesion of the mixture are avoided.

Fel Bovis Purificatum ; Purified Ox-gall.—Fresh ox-gall contains considerable mucilaginous matter which, upon concentration of the former, renders the inspissated mass tough and unmanageable—this can be removed with alcohol; and as liquid fresh bile is unfit for internal administration, purification is necessary. The U. S. Pharmacopœia directs that fresh ox-gall be evaporated on a water-bath to one-third its volume, and then mixed with an equal bulk of alcohol and set aside in a covered vessel for three or four days; the clear solution is then decanted, the remainder filtered, and the mixed liquids evaporated to a pilular consistence.

A simple test of the quality of purified ox-gall is to dissolve it in water, when a clear solution should result, which should remain transparent upon addition of an equal volume of alcohol.

THE OFFICIAL EXTRACTS.

The Pharmacopœia recognizes 27 extracts, of which 18 are directed to be made from the drug direct and the remaining 9 by evaporation of the official fluidextracts of the respective drugs. With the exception of extract of Indian cannabis, this latter method is directed in every case where the fluidextract of the drug is made with the same menstruum which is intended to be used for the corresponding extract. The plan is convenient for the preparation of extracts in small quantities, and perfectly proper, since from 80 to 90 per cent. of the liquid constituting the fluidextract has not been subjected to heat at all, and is therefore practically identical with a percolate freshly obtained.

According to the menstrua used for extraction of the drugs direct or for preparation of the fluidextract to be evaporated, the official extracts may be divided into the following classes:

Made with official alcohol: cimicifuga, Indian cannabis, and and physostigma.

Made with a mixture of alcohol 4 volumes, water 1 volume: euonymus, rhubarb, and scopola.

Made with a mixture of alcohol 3 volumes, water 1 volume: leptandra and sumbul.

Made with a mixture of alcohol 5 volumes, water 2 volumes: ergot.

Made with a mixture of alcohol 2 volumes, water 1 volume: belladonna leaves, hyoscyamus, and stramonium.

Made with official diluted alcohol: colocynth and digitalis.

Made with a mixture of alcohol 12½ volumes, water 87½ volumes: cascara sagrada and taraxacum.

Made with water: aloes, colchicum corm (with addition of acetic acid), gentian, glycyrrhiza (with addition of ammonia water), hematoxylon, krameria, malt, opium, and quassia.

Made with a mixture of water 13 volumes, acetic acid (36 per cent.) 5 volumes, the resulting extract being subsequently treated with a mixture of alcohol 3 volumes, water 1 volume, and the insoluble portion rejected: nux vomica.

ALPHABETICAL LIST OF OFFICIAL EXTRACTS.

Showing the fineness of the powdered drug, the menstruum used, the required moisture, and the average yield.

Name.	Fineness of Powder.	Menstruum.	Quantity of menstruum to moisten 1000 Gm. of the drug.	Degree of Packing.	Reserve	Average yield.
Extractum						
Aloes	. . .	Boiling Water.	. . . .	. . . .	. . .	50 p. ct.
Belladonnæ Foliorum . .	No. 60	Alcohol 2 vols. Water 1 vol.	400 Cc.	Firm	900 Cc.	
Cannabis Indicæ	" 20	Alcohol	300 "	"	. . .	12½ "
Cimicifugæ . .	Made by evaporation of Fluidextract of Cimicifuga, and subsequent incorporation of finely powdered Licorice Root.					
Colchici Cormi .	No. 60	Acetic Acid 35 vols. Water 150 "	500 Cc.	Moderate	. . .	22 p. ct.
Colocynthidis .	" 20	Diluted Alcohol	. . . .	. . .	From pulp From pulp & seed	40 " 15 "
Colocynthidis Compositum	This extract is a mixture of 160 parts Extract of Colocynth, 500 parts of Purified Aloes, 140 parts each of Resin of Scammony and Soap, and 60 parts of Cardamom.					
Digitalis	Made by evaporation of Fluidextract of Digitalis				. . .	25 p. ct.
Ergotæ	No. 40	Alcohol 5 vols. Water 2 "	500 Cc.	. . . .	. . .	12½ "
Euonymi . . .	Made by evaporation of Fluidextract of Euonymus, and subsequent incorporation of finely powdered Licorice Root.					
Gentianæ	No. 20	Water	400 Cc.	. . . .	. . .	33 p. ct.
Glycyrrhizæ Purum . . .	" 20	Ammonia water 5 vols. Water 100 "	1000 "	Moderate	. . .	20 "
Hæmatoxyli . .	Rasped	Water	. . . .	. . . .	. . .	10 "
Hyoscyami . . .	Made by evaporation of Fluidextract of Hyoscyamus.					
Krameriæ . . .	No. 40	Water	300 Cc.	. . . .	. . .	12 "
Leptandræ . .	Made by evaporation of Fluidextract of Leptandra, and subsequent incorporation of finely powdered Licorice Root.					
Malti	No. 12	Water	. . . .	. . . .	. . .	60 p. ct.
Nucis Vomicæ .	" 20	Acetic Acid 5 vols. Water 13 "	400 Cc.			
Opii	Very fine powder	Water.				
Physostigmatis .	No. 80	Alcohol	400 "	Firm	900 Cc.	
Quassiæ	" 20	Water	400 "	"		
Rhamni Purshianæ	" 60	Alcohol 12½ vols. Water 87½ "	400 "			
Rhei	Made by evaporation of Fluidextract of Rhubarb. . . .				. . .	40 "
Scopolæ	" " " Scopola.					
Stramonii . . .	" " " Stramonium.					
Sumbul	" " " Sumbul.					
Taraxaci	No. 30	Alcohol 12½ vols. Water 87½ "	250 Cc.	. . . .	. . .	15 "

Classified according to their consistence, the official extracts may be divided as follows:

Dry Extracts: Aloes, cascara sagrada, cimicifuga, colocynth, compound colocynth, euonymus, hematoxylon, krameria, leptandra, nux vomica, opium, physostigma, and quassia.

Pilular Extracts: Belladonna leaves, colchicum corm, digitalis, gentian, hyoscyamus, Indian cannabis, licorice (purified), rhubarb, scopola, stramonium, sumbul, and taraxacum.

Soft Extracts: Ergot and malt.

SPECIAL REMARKS.

Extractum Aloes; Extract of Aloes.—Since the official title Aloe includes the inspissated juice derived from different species of the plant, the extract may be made from any of the commercial varieties. It is probable that the so-called Barbadoes or Curaçao aloes is chiefly employed. The large proportion of water ordered by the Pharmacopœia is for the purpose of avoiding the admixture of resin; a concentrated aqueous solution of aloes retains in solution the resin present, whereas a dilute solution deposits it on cooling. The extract does not yield a perfectly clear solution with water, as complete separation of resinous matter is impossible. The extract, when properly made, is brittle and easily converted into a yellow-brown powder.

Extractum Belladonnæ Foliorum; Extract of Belladonna Leaves.—The official title of this extract is rarely used by physicians, the more familiar term *Extractum Belladonnæ* being employed in prescription-writing. In Great Britain the name *Extractum Belladonnæ Alcoholicum* is applied to an alcoholic extract of belladonna root, a preparation differing from our extract, both in appearance and strength, having a brown color and containing only about two-thirds as much alkaloid. *Extractum Belladonnæ Viride* of the British Pharmacopœia, formerly known as Extractum Belladonnæ, is the inspissated juice of fresh belladonna herb.

The U. S. Pharmacopœia directs that extract of belladonna leaves shall contain 1.4 per cent. of total alkaloids, to be determined by titration with volumetric acid solution, and if found to contain a larger proportion, it must be brought to the official standard by the addition of a sufficient quantity of powdered sugar of milk, which should be thoroughly incorporated.

The necessary quantity of diluent may be found by calculation as follows: Suppose the extract is found to contain 1.56 per cent. of alkaloids, then each Gm. contains 0.0156 Gm. (instead of 0.014 Gm., the prescribed standard), and will require the addition of 0.114 Gm. of sugar of milk, for $0.014 : 0.0156 :: 1 : x$ ($x=1.114$), where x represents the quantity of official extract that corresponds to, or can be made from, 1 Gm. of the assayed extract; then $1.114 - 1 = 0.114$. This method of calculation can also be applied to other official standardized pilular extracts.

Extractum Cannabis Indicæ; Extract of Indian Cannabis.—Owing to the variable character of commercial Indian hemp, the extract is at times of unsatisfactory quality, and in the absence of constituents which admit of chemical assay, physiological tests would seem to be desirable to determine the true value of the preparation. The extract is rich in resin, has a blackish-green color, and a peculiar, rather unpleasant heavy odor. It is soluble in alcohol, ether, chloroform, oil of turpentine, and fixed oils. Its alcoholic solution is precipitated by solution of potassium or sodium hydroxide, the resin being insoluble in alkalies.

While chiefly administered in pill-form, extract of Indian cannabis is sometimes prescribed in mixtures and can then be best kept in suspension by dissolving it in a small quantity of expressed oil of almond and emulsifying the solution with the aid of acacia.

Extractum Cimicifugæ; Extract of Cimicifuga.—Since the residue obtained by evaporation of fluidextract of cimicifuga consists wholly of resinous matter, it is admirably adapted to the pulverulent form, which is easily maintained by the addition of finely-powdered licorice root. The Pharmacopœia directs that 25 Gm. of powdered extract shall be made from 100 Cc. of the fluidextract, and thus it represents 4 times its weight of the crude drug.

Extractum Colchici Cormi; Extract of Colchicum Corm.—Although the official title of this extract has been changed, the name extract of colchicum root will no doubt continue in use among physicians and others. The British extract of colchicum is the inspissated juice of the corm freed from feculent matter. The Pharmacopœia requires that the official extract of colchicum corm shall contain 1.4 per cent. of colchicine, to be determined gravimetrically. If the extract be found by assay to contain more than this proportion of alkaloid, sufficient powdered sugar of milk should be incorporated to reduce it to the official standard.

Extractum Colocynthidis; Extract of Colocynth.—In order to avoid the fixed oil which is present in the seeds, the Pharmacopœia directs that only the pulp of the colocynth shall be used; maceration and expression are preferred to percolation, on account of the spongy character of the material. The yield of extract varies from 40 to 50 per cent. if made from good pulp; if calculated for the well-dried whole fruit, it ranges from 14 to 20 per cent. Many manufacturers allow the seeds to remain in the fruit, being careful not to have them crushed during the grinding. The presence of fixed oil in the extract would prevent evaporation to dryness and subsequent reduction to powder.

Extractum Colocynthidis Compositum; Compound Extract of Colocynth.—Since a perfectly homogeneous preparation cannot be obtained by simply mixing the ingredients in fine powder, the Pharmacopœia very properly directs that an intimate mixture shall be effected with the aid of heat and alcohol; when the alcohol has been evaporated and the mass becomes brittle, the powdered cardamom is incorporated and the vessel covered until cold, so as to avoid loss of volatile oil. The dry compound extract is finally reduced to powder. It contains half its weight of purified aloes, 16 per cent. of dry extract of colocynth, 14 per cent. each of soap and resin of scammony, and 6 per cent. of cardamom.

Extractum Ergotæ; Extract of Ergot.—The official process for the preparation of this extract is practically identical with that of the British and Swiss Pharmacopœias. The extract represents 8 times its weight of crude ergot and is of the consistence of thick honey. Having been freed from inert matter and being perfectly soluble in water, it is admirably adapted for hypodermatic use. The presence of 10 per cent. of glycerin prevents the extract from drying out and thus preserves the relation between the extract and the crude drug.

Extractum Euonymi; Extract of Euonymus, also known as **Extract of Wahoo.**—Fluidextract of euonymus upon evaporation yields a residue rich in resin which is readily powdered, and must then be mixed with sufficient finely powdered licorice root to bring the finished product up to the official standard, which demands that the extract shall represent 4 times its weight of the crude drug.

Extractum Gentianæ; Extract of Gentian.—All of the valuable bitter principles of gentian are soluble in cold water, while much inert matter is avoided by the use of this menstruum; when hot water is employed, the yield of extract is vastly increased on account of the large quantity of pectin compounds taken up. The object of boiling the cold-water percolate, as directed in the U. S. Pharmacopœia, is to coagulate the albuminous matter, after removal of which the extract obtained forms an almost clear solution with water. To judge from the tough condition and imperfect solubility of many commercial extracts of gentian, manufacturers must frequently resort to heat in the exhaustion of the drug. With cold water, gentian yields about 30 per cent. of extract, which can be increased to 50 or 60 per cent. with hot water; the United States, German, French, and Swiss Pharmacopœias, all direct cold water; but the British Pharmacopœia, strange to say, recommends infusion for two hours and then boiling for fifteen minutes, followed by expression.

Extractum Glycyrrhizæ Purum; Pure Extract of Glycyrrhiza.—Commercial extract of licorice is prepared in a crude way with boiling water, the decoction being evaporated and then mixed with powdered licorice root, starch, and other substances to give it the necessary firm consistence. It occurs both in the form of mass and rolls or sticks, and also in powder, but is not suited for liquid preparations on account of the large amount of insoluble matter present; hence the Pharmacopœia directs the preparation of a completely soluble extract, officially designated as pure extract of glycyrrhiza. The addition of ammonia water to the menstruum is intended to dissolve any glycyrrhizin which may be present in the powdered drug in an insoluble condition.

Extractum Hæmatoxyli; Extract of Hematoxylon, also known as **Extract of Logwood.**—The medicinal value of logwood lies in its astringent principle, which cannot be entirely extracted with cold water; hence boiling is officially directed. It is important that all contact with metal be avoided on account of the tannin. The extract should yield a clear, purplish-red solution with water. Extract of hematoxylon is well adapted for the dry condition, as it is non-hygroscopic; its taste is sweetish and afterward astringent. The commercial extracts of logwood sold in boxes are not suitable for medicinal purposes, being only partly soluble in cold water.

Extractum Hyoscyami; Extract of Hyoscyamus.—As henbane is very variable in its alkaloidal content, and at times of poor quality, a carefully standardized fluidextract only should be used in the preparation of the extract, especially as the average yield of pilular extract is equal to about 24 per cent. The Pharmacopœia requires that extract of hyoscyamus shall contain 0.3 per cent. of total alkaloids, to be determined by titration with volumetric acid solution. If the extract should be found to contain a larger percentage of alkaloids, sufficient powdered sugar of milk must be incorporated to reduce it to the official standard. For method of finding the necessary amount of diluent, see Extract of Belladonna Leaves. The extracts of hyoscyamus of the British and German Pharmacopœias are the inspissated juice of fresh flowering herb. The first-named is recognized under the official title Extractum Hyoscyami Viride. Cubical crystals sometimes found in British extracts of belladonna and hyoscyamus have upon examination proved to be potassium chloride.

Extractum Krameriæ; Extract of Krameria, also known as **Extract of Rhatany.**—Cold water is an excellent solvent for the particular tannin present in rhatany, upon which the astringency of the drug depends; hot water will yield a larger percentage of extract, but this will not form a complete solution with water, while the cold water extract is soluble, and with the addition of sugar forms a perfectly clear liquor. A very weak alcoholic menstruum is said also to furnish an increased yield of extract, but with results similar to those produced by hot water. Decided astringency and a perfectly clear solution with warm water and sugar are indications of a well-prepared extract.

Extractum Leptandræ; Extract of Leptandra.—Although the yield of dry extract obtained by evaporation of the fluidextract of leptandra rarely exceeds 12 or 12½ per cent., thus leaving a large quantity of diluent available for establishing the official standard of strength, 1 Gm. of the powdered extract to represent 4 Gm. of the crude drug, licorice root alone has been found satisfactory for maintaining the pulverulent condition of the official extract. The finished product should be kept in tightly stoppered bottles, in a cool, dry place, to avoid caking of the powder.

Extractum Malti; Extract of Malt.—Since diastase, the chief active constituent of malt, is destroyed by a temperature approaching that of boiling water, it is essential that the temperature prescribed in the official process of manufacture be not exceeded. Evaporation of the infusion at a low temperature in a vacuum apparatus is always to be preferred, the average yield being about 60–65 per cent. of extract. Extract of malt is a brown-yellow thick liquid or semifluid mass, having a slight peculiar odor, a sweet taste, and an acid reaction toward litmus paper.

The diastasic value of extract of malt is determined by its power of converting starch into dextrose, and the following method may be employed for comparative testing of different malt extracts, that extract capable of converting the largest amount of starch within a given time, under like conditions, being considered the best: Dissolve 5 Gm. of extract of malt in sufficient distilled water to yield 100 Cc. of solution; of this, add 5 Cc., representing 0.25 Gm. of the extract, to 250 Cc. of cold starch mucilage (prepared by dissolving 30 Gm. of Bermuda arrowroot in 1000 Cc. of boiling distilled water) and keep the mixture at a temperature of 55° to 60° C. (131°–140° F.) for 30 minutes; then stop the diastasic action by raising the temperature to 100° C. (212° F.) or by addition of 2 or 3 Cc. of a 10 per cent. sodium hydroxide solution, and dilute the mixture to a given volume by addition of water. Titrate an aliquot part of the liquid with Fehling's Solution (alkaline cupric tartrate volumetric solution, U. S. P.) and ascertain the amount of dextrose present, from which deduct the amount found in a corresponding amount of the extract of malt by previous titration with Fehling's Solution; the difference indicates the amount of sugar produced by the diastase present in the extract. Each Cc. of Fehling's Solution corresponds to 0.005 Gm. of anhydrous dextrose, or 0.0045 Gm. of starch converted thereinto.

Extractum Nucis Vomicæ; Extract of Nux Vomica.—The object of exhausting the drug with 10 per cent. acetic acid is to avoid extraction of the fixed oil present in the seed, the subsequent removal of which before the extract can be powdered, is a tedious operation. A coarse powder is preferable in order to avoid impaction of the mass, since under the influence of the watery menstruum the powder rapidly swells. Unfortunately the acetous menstruum also extracts considerable inert matter, which by increasing the yield of dry extract may render the standardization of the powder impossible, or at least difficult, because the larger the yield of extract, the smaller must be the percentage of alkaloids in the same. In the author's experience from 35 to 40 per cent. of dry extract has been obtained by exhausting nux vomica with the official menstruum; and assuming the average strychnine content of prime nux vomica to be 1.5 per cent., such an extract would contain from 3.75 to 4.22 per cent. of strychnine and allow no addition of diluent to preserve the pulverulent condition, being already below the prescribed standard. The Pharmacopœia therefore very properly directs that the concentrated liquid shall be diluted with 3⅓ times its volume of alcohol, whereby the inert matter extracted by the acid menstruum is precipitated, the hydro-alcoholic liquid retaining the alkaloids present in solution as acetates. After washing the precipitate thoroughly with a mixture of alcohol and water, as prescribed, the solution is evaporated to dryness and a small quantity of the powdered extract is assayed; from the results obtained the quantity of sugar of milk is calculated necessary to add to the remainder of the powder, so that the finished product shall contain the prescribed amount of strychnine, namely 5 per cent.

Thus, if 2 Gm. of the powdered extract should be found to contain 0.130 Gm. of strychnine, or 6.5 per cent., then each Gm. of the remaining powder requires the addition of 0.300 Gm. of sugar of milk to reduce the strength to that of the official standard of 5 per cent., for $0.05 : 0.065 : 1 : x$ $(x = 1.300)$, where x represents the weight of official extract corresponding to 1 Gm. of the extract assayed. Then $1.300 - 1 = 0.300$ in grammes.

Powdered extract of nux vomica is very susceptible to moisture and heat, and readily cakes unless preserved in tightly stoppered bottles in a cool, dry place. The present extract is weaker than that formerly official, which latter contained 15 per cent. of total alkaloids and since the proportion of strychnine present in the total alkaloids varies from 45 to 55 per cent., this would correspond to from 6.75 to 8.25 per cent. of strychnine, as compared with the present official standard of 5 per cent. The British extract of nux vomica is of pilular consistence, but of the same strychnine content as our own.

Extractum Opii; Extract of Opium.—Opium is easily exhausted with cold water, but instead of triturating the mixture of opium and water occasionally during twelve hours, it is better to rub the opium into a smooth paste with water in a mortar, wash this carefully into a flask or bottle, add the remainder of the water, cork the flask or bottle, and shake vigorously every hour or two; agitation is more easily accomplished and is more beneficial to the extraction of the soluble principles. The magma on the filter should be slowly percolated with water until the liquid is nearly colorless and only faintly bitter. After concentration of the percolate to about twice the weight of opium used, the moisture and morphine present are determined, in order to ascertain the amount of sugar of milk which must be added to the syrupy extract, so that, upon complete drying, it shall yield a powder containing 20 per cent. of crystallized morphine.

Suppose the thick syrupy liquid is found to contain 72 per cent. of moisture and to yield 7 per cent. of crystallized morphine: then each Gm. of the liquid will require the addition of 0.07 Gm. sugar of milk, so that when evaporated to dryness and powdered the extract shall contain the prescribed quantity, 20 per cent., of morphine, as shown by the following calculation: As the syrupy liquid contains 72 per cent. of moisture, 100 Gm. will yield $100 - 72$, or 28, Gm. of dry extract, and the original morphine content of 7 per cent. (or 7 Gm. in 100 Gm.) will be increased to 25 per cent. in the dry extract, because no morphine is lost, and 7 Gm. is 25 per cent. of 28 Gm. Now, according to the rule for adjustment of percentages, given on page 73, multiply the given quantity by the given percentage and divide by the required percentage, or 28 × 25 = 700, and 700 ÷ 20 = 35; hence the 28 Gm. of dry extract, representing 100 Gm. of the syrupy liquid, will yield 35 Gm. of powdered extract of the official standard, yielding 20 per cent. of crystallized morphine. The difference, then, between 28 Gm. and 35 Gm. (or 7 Gm.) is the quantity of sugar of milk required for 100 Gm. of the syrupy liquid, or 0.07 Gm. for 1 Gm.

Proof: 1 Gm. of the syrupy liquid yielding 0.07 Gm. of crystallized morphine, when mixed with 0.07 Gm. of sugar of milk, upon evaporation to dryness will yield 0.35 Gm. of dry extract still containing the original quantity of morphine (0.07), and 0.07 Gm. is 20 per cent., or ⅕, of 0.35 Gm., for 0.07 divided by 0.35 = 0.20.

Extractum Physostigmatis; Extract of Physostigma, also known as **Extract of Calabar Bean.**—Like all seeds, physostigma contains considerable fat, which is extracted by the alcoholic menstruum, and hence it is not possible to produce a perfect pilular or powdered extract without the addition of some diluent. While sugar of milk, if added, produces a good pilular mass, as directed in the British Pharmacopœia, powdered licorice root is a better absorbent and yields quite a fair powdered extract. The Pharmacopœia requires that the finished extract shall contain 2 per cent. of ether-soluble alkaloids, and if the extract is found to contain a larger proportion of the alkaloids, sufficient finely powdered licorice root must be added to reduce the strength to the official standard. The necessary quantity of licorice root to be added to each Gm. of the dry extract may be found by the same method of calculation as given under Extract of Nux Vomica.

Extractum Quassiæ; Extract of Quassia.—Owing to the tendency of this extract, if in pilular condition, to become tough in the course of time, it seems preferable to have it in the powdered form; and since the yield of extract obtained by exhausting quassia with cold water is small, rarely above 4 per cent., the Pharmacopœia directs dilution with sufficient sugar of milk so that the finished product shall represent [illegible] times its weight of the crude drug. In this condition the extract is well adapted for all purposes, is perfectly soluble in water, and keeps well.

Extractum Rhamni Purshianæ; Extract of Cascara Sagrada.—Although cold water is capable of extracting all the medicinal virtues of cascara sagrada bark, a weak alcohol (about 12 per cent.) menstruum is preferred, so as to avoid fermentative changes during the prolonged maceration and percolation, especially in warm weather. The yield of dry extract [illegible] from [illegible] to [illegible] per cent., and after admixture with sufficient [illegible], [illegible], so that the finished product shall represent [illegible] times its weight of the crude drug, the powdered extract keeps well.

Extractum Rhei; Extract of Rhubarb.—When the official fluidextract of rhubarb is evaporated to dryness it yields from 35 to 42 per cent. of residue, which can easily be reduced to powder, and keeps admirably if mixed with sufficient powdered licorice root to represent twice its weight of the crude drug. Such a powdered extract corresponds very nearly to the yield of pilular extract obtainable from the fluidextract directed by the Pharmacopœia and is preferable to the latter for dispensing purposes, since the pilular extract is apt to become tough and dry with age unless some glycerin be incorporated with it.

Extractum Scopolæ; Extract of Scopola.—This extract, which is practically identical in composition and medicinal effects with an extract made from belladonna root, is officially recognized for the purpose of permitting its use in plasters. The yield of extract in pilular form is about 16 to 20 per cent. and the Pharmacopœia requires that it shall contain 2 per cent. of mydriatic alkaloids, to be determined by titration with volumetric acid solution. If the extract be found to be above the prescribed strength, sufficient powdered sugar of milk must be added to reduce it to the official standard. The necessary quantity of sugar of milk can be found by calculation, as explained under Extract of Belladonna Leaves.

Extractum Stramonii; Extract of Stramonium.—Since the leaves are the only part of the stramonium plant officially recognized, the present extract is rich in green coloring-matter. It is prepared like extract of hyoscyamus, but is required to contain 1.4 per cent. of alkaloids, to be determined by titration with volumetric acid solution. If found to be above the prescribed strength, it must be mixed with sufficient powdered sugar of milk to reduce it to the official standard. The average yield of extract of stramonium leaves is about 20 per cent. On account of the large proportion of resinous matter in the leaves it is essential that the fluidextract be constantly stirred during evaporation, especially toward the end of the operation, otherwise a granular product may result from the separation of resin as the alcoholic strength of the liquid changes.

Extractum Sumbul; Extract of Sumbul.—It is impossible to obtain a perfect pilular extract, in the case of sumbul, on account of the peculiar nature of the resin and oil present in the root. The yield of extract is about 15 per cent.

Extractum Taraxaci; Extract of Taraxacum, also known as **Extract of Dandelion.**—Although this extract was formerly directed to be prepared by expression and evaporation of the juice of the root freshly gathered, it is doubtful whether this plan was followed to any great extent, and, moreover, no provision was made for the removal of the starchy and albuminous constituents of the juice. The exhaustion of the ground taraxacum with a weak alcoholic (about 12 per cent.) menstruum insures a complete extraction of the medicinal virtues, without much inert matter, the resulting extract yielding a nearly clear solution with water. Absence of a bitter taste in the last portions of the percolate indicates complete exhaustion of the drug.

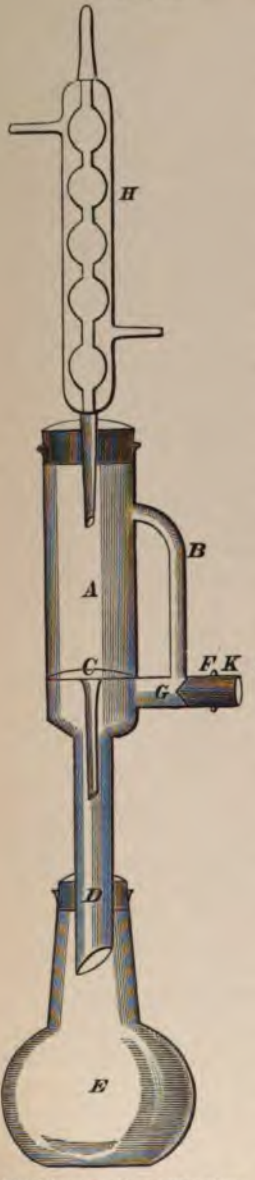
CHAPTER XXIV.

OLEORESINS AND RESINS.

OLEORESINS.

SOLUTIONS of this class represent the medicinal virtues of the drugs from which they are made, in a more concentrated form than is possible in any other. They possess the power of self-preservation, and in this respect are superior to fluidextracts. Oleoresins consist chiefly of fixed or volatile oils associated with resin and other constituents; those officially recognized, with one exception, are all prepared by the same process, which consists in slowly percolating the drug in fine powder, with acetone, to exhaustion, recovering the greater part of the acetone by distillation, and finally removing the remaining acetone by spontaneous evaporation. The percolation of drugs with acetone requires the use of special apparatus (see page 134) to prevent loss of the volatile solvent, and several attempts have been made to economize menstruum by repeatedly using the same liquid until the material is exhausted, the best device for this purpose being the ether extraction apparatus designed by Prof. Flückiger, illustrated in Fig. 215. The extractor *A* passes by means of the tube *D* through a cork into the receiving flask *E;* at *C* is a septum or disk, upon which the material to be extracted is packed, and which communicates by means of a small funnel-shaped tube with *D*. The lateral tube *BF* passes into the tube *G*, which is provided with a properly cut cork, *K*, so that the acetone vapor may pass from the receiving bottle to a spiral condenser, *H*, fitted by means of a cork to the top of the extractor; the acetone vapor can also be made to pass upward through the powder by pushing the cork deeper into the tube *G*, thus closing the orifice of the lateral tube *BF*. A loose pledget of cotton is placed in the funnel tube at *C*, or a piece of filter paper is placed over the small opening to prevent the material from passing down. The whole apparatus may be made of any convenient size, of glass or tinned copper, and when in use the receiving flask is placed in warm water, for the purpose of vaporizing the acetone, which is condensed above the extractor and drops back upon the powder, the process being continued until the material is exhausted. Another desirable feature of this apparatus is the recovery of the acetone from the marc when the extraction of the drug has been completed. The lateral communication between *D* and *BF* is closed by means of the cork, and, applying a cold wet sponge to the receiving flask, the acetone vapor therein is condensed and a partial vacuum produced, which withdraws all the ether from the marc in the percolator above.

FIG. 215.



Flückiger's ether-extraction apparatus.

Experience has shown that when 2 Cc. of percolate have been obtained for each Gm. of drug used, the latter will be practically exhausted, therefore percolation beyond this point is unnecessary; with the continuous extraction apparatus, half the quantity of acetone can be made to accomplish the same results.

Some care is necessary in the recovery of acetone by distillation, as official acetone, which is directed to be used in the process, boils at 56.5° C. (133.7° F.); the recovered acetone should be but very slightly impregnated with the odor of volatile oil, and may be used for a subsequent operation. Oleoresins are not used to any great extent at present, and are rarely made by the pharmacist himself; small quantities for use in prescriptions may be conveniently obtained by percolating some of the finely powdered drug in the barrel of a glass syringe and allowing the acetone to evaporate in a warm place. The yield of oleoresins ranges from 5 to 60 per cent. for different drugs, and their consistence varies from liquid to a soft solid, dependent upon the amount of resin present.

The use of acetone in the manufacture of oleoresins was first suggested by Beringer in 1892, and has been found very satisfactory. It can now be obtained of great purity, 99.5 per cent., at a moderate price, and its chief advantage over ether, the menstruum formerly employed, lies in its higher boiling-point and consequent lesser volatility. Oleoresins prepared with acetone have been found entirely soluble in ether and do not appear to differ in any way from those made with ether. Drugs exhausted with acetone, when subsequently percolated with ether, have been found to yield nothing of value to the latter solvent.

The Pharmacopœia recognizes 5 oleoresins prepared with acetone and 1 with alcohol, and in every case, with one exception, the drug is packed firmly into the percolator, previous moistening being unnecessary. On account of the large proportion of resin in lupulin this drug must be packed lightly, otherwise the mass will become impacted. The following is an alphabetical list of the official oleoresins, showing the fineness of powder used and the average yield:

LIST OF OFFICIAL OLEORESINS.

Latin Name.	English Name.	Fineness of Powder.	Average Yield.
Oleoresina Aspidii	Oleoresin of Aspidium	No. 60	15 per cent.
Oleoresina Capsici	Oleoresin of Capsicum	" 60	12 " "
Oleoresina Cubebæ	Oleoresin of Cubeb	" 30	22 " "
Oleoresina Lupulini	Oleoresin of Lupulin		60 " "
Oleoresina Piperis	Oleoresin of Pepper	" 60	6.5 " "
Oleoresina Zingiberis	Oleoresin of Ginger	" 60	6. " "

Special Remarks.

Oleoresin of Aspidium, also known as **Oleoresin of Male Fern.**—This preparation is known also by the names *oleoresina filicis, extractum filicis æthereum,* and *oleum filicis maris.* As the root rapidly deteriorates upon keeping, only that having a fresh green color should be used. The oleoresin of male fern generally deposits, on standing, a granular crystalline substance largely composed of filicic acid, upon which depends the activity of the preparation; hence the necessity for thoroughly incorporating the deposit before dispensing the oleoresin. By percolation with acetone the drug has yielded as much as 18 per cent. of oleoresin. This preparation is recognized in the British Pharmacopœia as Extractum Filicis Liquidum, and in the German Pharmacopœia as Extractum Filicis.

Oleoresin of Capsicum.—Owing to the large amount of fat present in capsicum it is not desirable to carry percolation to complete exhaustion; experience, in fact, has taught that, if collected slowly, 150 Cc. of percolate will have practically exhausted 100 Gm. of the drug, and that further treatment simply loads the percolate with fatty matter. Oleoresin of capsicum is a dark, brownish-red liquid, which, shortly after being made, deposits granular fat; this is best removed by decanting the clear liquid and straining the residue, or washing the deposit rapidly with a little acetone. Although the average yield of oleoresin has been reported as not over 5 or 6 per cent., from 12 to 16 per cent. of a very excellent preparation has very frequently been obtained.

Oleoresin of Cubeb.—Cubeb yields all its medicinal virtues to alcohol as well as acetone; very satisfactory oleoresin has been made with alcohol alone, and this menstruum is now used by many manufacturers. In Germany the oleoresin is officially recognized under the name *Extractum Cubebarum,* and is prepared with a mixture of equal volumes of ether and alcohol. All oleoresin of cubeb deposits, upon standing, waxy matter and a crystalline body, cubebin, which, as the Pharmacopœia directs, should be rejected, only the liquid portion being dispensed. It is of a green or brownish-green color, and when made with acetone has been obtained to the extent of 25 per cent.

Oleoresin of Ginger.—When made from uncoated (Jamaica) ginger the yield of oleoresin is less than from coated ginger, and is also lighter in color, thinner, and of a more agreeable flavor. The name *piperoid* has sometimes been applied to this preparation. From coated ginger as much as 10 per cent. of oleoresin has been obtained, while from Jamaica ginger the yield rarely exceeds 6 per cent.

Oleoresin of Lupulin.—Lupulin is very rich in resin, hence a large yield of oleoresin is to be expected; it is of a reddish-brown color and has the consistence of a soft solid extract. While the average yield is about 60 per cent., as much as 70 per cent. has been obtained, with both ether and acetone, by complete exhaustion.

Oleoresin of Pepper.—Commercially this preparation is known also as *oil of black pepper*, which latter, however, is usually obtained as a by-product in the manufacture of piperin. Oleoresin of pepper, when first made, deposits piperin in crystalline form, which is separated by straining, leaving a thick, very black liquid. The yield with ether or acetone rarely exceeds 6.5 per cent.

RESINS.

Under the title *Resinæ* the Pharmacopœia recognizes 4 preparations, 1 of which, however, is simply a residuary product obtained in the distillation of the volatile oil from a natural oleoresin. For the remaining 3 an official process of manufacture is given, alcohol being used as a solvent in each case; the resin is obtained by pouring a concentrated alcoholic tincture of the respective drugs into cold water and subsequently washing the precipitate repeatedly with water.

ALPHABETICAL LIST OF THE OFFICIAL RESINS.

Latin Name.	English Name.	Mode of obtaining.
Resina	Rosin	Residue left after distillation of the volatile oil from Turpentine.
Resina Jalap	Resin of Jalap	By pouring a concentrated alcoholic tincture of Jalap into cold water.
Resina Podophylli	Resin of Podophyllum	By pouring a concentrated alcoholic tincture of Podophyllum into cold water acidulated with hydrochloric acid.
Resina Scammonii	Resin of Scammony	By pouring a concentrated alcoholic tincture of Scammony into cold water.

Special Remarks.

Resin of Jalap.—The amount of resin in jalap root varies considerably, ranging from 6 to 18 per cent., and it is not always possible to find commercial jalap, which exceeds the official requirement of *not less than 8 per cent.* of resin, although prime lots yielding from 12 to 15 per cent. are occasionally met with. Resin of jalap is soluble in alcohol in all proportions, the solution having a slight acid reaction to litmus paper; it is also soluble slowly in 5 times its weight of 10 per cent. ammonia water, but is insoluble in fixed and volatile oils. The Pharmacopœia requires that not more than 10 per cent. of the resin shall be soluble in ether, and not more than 35 per cent. in chloroform, and that if its solution in ammonia water be acidified with hydrochloric acid, only a slight turbidity shall appear, showing the absence of rosin, guaiac, and other resins. The presence of common rosin may also be detected by solubility in oil of turpentine and by gelatinization upon cooling a solution made by digesting the suspected resin in 10 parts of ammonia water at 80° C. (176° F.). Since resin of jalap has a slightly acrid but not bitter taste, an adulteration with aloes may be suspected if a pronounced bitter taste is observed. If resin of jalap be moistened with alcohol and then with a solution of ferric chloride, a green color should not be developed, nor should a blue color be observed if the inner surface of a fresh potato paring be rubbed with the resin, otherwise guaiac is present. That portion of jalap resin insoluble in ether, when dissolved in caustic alkali solution, is not reprecipitated upon addition of an acid; this property distinguishes jalap resin from other resins except that of scammony, and from the latter it differs in its insolubility in ether and oil of turpentine. While resin of scammony might become accidentally mixed with jalap resin, it would never be added as an adulterant, since it is far more expensive.

Resin of jalap may be obtained free from color by treatment with animal charcoal; the best plan is to mix the charcoal with the powdered jalap before percolation, and also to pass the percolate through animal charcoal.

Resin of Podophyllum.—The object of adding hydrochloric acid to the water before adding the alcoholic solution is simply to facilitate the separation of the resinous matter. The yield of resin of podophyllum rarely exceeds 4 or 5 per cent., and its color should be from grayish white to yellowish green, provided no heat higher than 35° C. (95° F.) is used in drying it. According to Prof. Lloyd, who has had large experience in the manufacture of this resin, the concentration of the alcoholic tincture should not be carried beyond a very thin syrup, the water into which it is poured should be ice-cold, and the washed resin should be dried *without* heat, by exposure to air in a cold place. Alum-water is sometimes used to effect precipitation of the resin, but it yields a yellow product of inferior quality. The Pharmacopœia requires that not less than 99 per cent.

of resin of podophyllum shall be soluble in alcohol, not less than 75 per cent. in ether, not less than 65 per cent. in chloroform, and not more than 25 per cent. in boiling water; also that upon incineration it shall not yield more than 0.7 per cent. of ash. The solubility of resin of podophyllum in ether varies from 50 to 85 per cent., depending upon the mode of its preparation, the better quality being most soluble and also lighter in color; according to F. B. Power, boiling water will dissolve about 80 per cent. of the resin if the treatment with fresh portions of the water be continued as long as anything is removed, but deposits most of it again on cooling. Resin of podophyllum forms a yellow liquid with solution of sodium or potassium hydroxide, from which it is reprecipitated by acids.

The name *podophyllin* is extensively applied in commerce to the resin, but does not always represent the official article.

Resin of Scammony.—The Pharmacopœia directs that this resin be prepared from the gum-resin scammony, and not from the root direct, as in the two preceding resins; hence treatment of the powder with boiling alcohol is directed instead of percolation. The yield of resin of scammony depends upon the quality of the gum-resin, and may vary from 70 to 90 per cent., alcohol taking up only about 2 per cent. of water-soluble matter, according to Prof. Markoe.

Resin of scammony is wholly soluble in ether and oil of turpentine, and is not precipitated by acids from its solution in caustic alkalies. It is very slowly acted upon by sulphuric acid, whereas common rosin is immediately turned intensely red; the presence of the latter can thus be detected. The resin of scammony can be distinguished from the gum-resin by not yielding a green emulsion when triturated with water. The Pharmacopœia requires that upon incineration resin of scammony shall not yield more than 1 per cent. of ash.

CHAPTER XXV.

COLLODIONS.

UNDER this head are recognized in the Pharmacopœia 4 solutions, the base of which is pyroxylin, or soluble gun-cotton (see Cellulose, Part III.), and the solvent, a mixture of alcohol and ether. Collodions are employed only for external medication, and owing to the very volatile character of the solvent they rapidly form a skin-like covering, or pellicle, when applied, which is impervious to water. Where a strong contractile coating is desired, the plain collodion is preferred, otherwise a less constringent and more comfortable covering is obtained by the addition of castor oil and Canada turpentine, as in the case of the official flexible collodion. For the purpose of medication, any substance soluble in ether may be added, such as iodine, iodoform, extract of Indian cannabis, salicylic acid, croton oil, mercuric chloride, veratrine, atropine, resorcin, pyrogallol, etc. Since pyroxylin is insoluble in water, the addition of the latter to collodion would cause immediate precipitation, hence all substances soluble only in water or alcohol and water, such as extract of belladonna, morphine sulphate, etc., are excluded from admixture. Collodions should always be preserved in tightly cork-stoppered bottles, in a cool place, remote from fire, on account of the ether present; care should also be taken that no collodion be allowed to remain on the lip or in the neck of the bottle after pouring out the liquid, to avoid "fixing" of the cork as the menstruum evaporates.

Collodions are best dispensed in small round-shouldered vials provided with a cork through which a camel-hair pencil has been passed and securely fastened; this avoids loss of material and drying of the collodion in the brush—a very annoying occurrence.

ALPHABETICAL LIST OF OFFICIAL COLLODIONS.

Latin Name.	English Name.	Composition.
Collodium	Collodion	Pyroxylin 4 Gm., Ether 75 Cc., Alcohol 25 Cc.
Collodium Cantharidatum	Cantharidal Collodion (Blistering Collodion)	Chloroformic Extract of Cantharides (representing 60 Gm. Cantharides) 15 Gm., Flexible Collodion 85 Gm.
Collodium Flexile	Flexible Collodion	Castor Oil 3 Gm., Canada Turpentine 5 Gm., Collodion 92 Gm.
Collodium Stypticum	Styptic Collodion	Tannin 20 Gm., Alcohol, 5 Cc., Ether 25 Cc., Collodion sufficient to make 100 Cc.

SPECIAL REMARKS.

Collodion.—If the pyroxylin has been carefully prepared, it should be perfectly soluble in the official menstruum, although a slight sediment of dirt, etc., occurs after the solution has been set aside for a few hours; from this the liquid can be carefully poured off, as filtration is impracticable. Anthony's collodion cotton, specially prepared for photographers' use, has been found very satisfactory.

Cantharidal Collodion.—The value of cantharidal collodion will depend upon the quality of the powdered cantharides used and the care with which it has been exhausted. Since chloroform is a very volatile menstruum, percolation must be conducted in a special apparatus (see Oleoresins), to avoid loss; the liquid is easily recovered by distillation on a water-bath, as chloroform boils at about 60° C. (140° F.). The extract dissolves readily in flexible collodion, by agitation, the finished product representing 60 per cent. of its weight of powdered cantharides, which makes it nearly twice as strong as the official cerate of cantharides.

Flexible Collodion.—The addition of Canada turpentine (Canada balsam, or balsam of fir) and castor oil imparts to collodion the property of forming a flexible pellicle which, while serving as an impervious covering to the part affected, yet permits of perfect freedom of motion.

Styptic Collodion.—Owing to the large proportion of tannin ordered in the formula for styptic collodion, it is necessary to use a small quantity of diluent—ether and alcohol—with which the tannin is thoroughly mixed before the final addition of collodion. Flexible collodion is not suitable in this case, as a constringent pellicle is desired. Any impurities from the tannin may be removed by rapidly straining the solution through gauze previously moistened with ether and alcohol.

CHAPTER XXVI.

EMULSIONS.

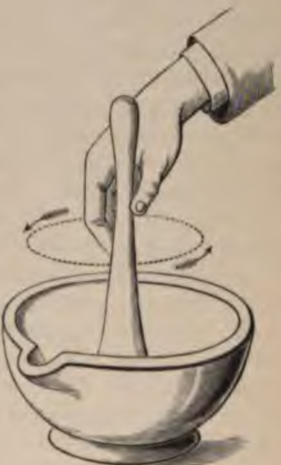
THE term "emulsion" is applied to a more or less permanent homogeneous liquid mixture composed of fatty, ethereal, or resinous substances and water, the former being suspended in a minutely divided state, which gives rise to a peculiar opaque and milk-like appearance. Nature provides types of true emulsions, in the form of milk, the natural food of all young mammalia, and the milk-like juices of certain plants from which the official and other gum-resins are obtained.

Emulsions prepared by pharmacists may conveniently be divided into natural and artificial; to the former class belong those which are made from seed or gum-resins, by simple trituration with water, Nature having provided the necessary emulsifying agent in intimate association with the oil or resin. Artificial emulsions are such as require the addition of some foreign body, by means of which the suspension of the oil or resin is made possible; to this class belong the majority of the emulsions prepared at the dispensing-counter. Fixed and volatile oils, as well as ether, chloroform, oleoresins, and resins, are suitable for exhibition in the form of emulsion, the suspension in water being accomplished by the aid of appropriate excipients, such as acacia, tragacanth, yolk of egg, casein, dextrin, Irish moss, gelatin, soap-bark, etc. Oil-yielding seeds and natural gum-resins contain albuminous and mucilaginous matter, by means of which the oil and resin can be brought into perfect suspension in water, and such emulsions approach more closely in character and stability to cows' milk, which may be looked upon as the most perfect emulsion known. The theory of emulsification is as follows: The insoluble liquid or solid, in a state of minute division, is completely surrounded or enveloped by the vehicle, consisting of water and excipient, and thus an opaque mixture is produced, from which the particles cannot separate by mere force of cohesion; such a condition can be obtained to perfection only by choice of a proper excipient, and for artificial emulsions none better than acacia has yet been found. Stability of artificial emulsions, while primarily dependent upon division of the insoluble liquid into minute globules, is also influenced to some extent by the density of the vehicle; thus sugar has been found to increase the suspending power of gum materially; to prevent the fermentative changes likely to arise in all aqueous vegetable solutions, alcohol or glycerin is frequently added to emulsions, in the proportion of 1 or 2 fluidounces for every pint.

With the exception of those composed of volatile oils or ethereal liquids, emulsions should always be made in a mortar, either of unglazed Wedgewood or hard porcelain, having a flat bottom, and, in the case of seed or gum-resin emulsions, one of deep shape provided with a hard-wood pestle is to be preferred, in order to avoid injury from the force often necessary in crushing and manipulating the material. For making gum-resin emulsions, the cleanest and best tears should be selected, as the commercial fine powders are unfit for this purpose, partly because they are inferior in quality, and partly because they have been so modified by drying that when triturated with water they form simply an ordinary mixture from which the powder separates rapidly on standing; this change is due to dehydration, whereby the natural association of gum and resin has been broken up and their intimate union destroyed. For seed emulsions, when no other proportions are specified, 1 part of seed is used to 10 parts of water, all dirt and dust being carefully removed, if necessary, by washing with cold water. In both cases the material is crushed into a coarse powder, and, after the addition of a small quantity of water, beaten into a perfectly smooth pasty mass; to this, the remainder of the water is then added in divided portions, triturating the mass thoroughly and keeping it well scraped from the pestle and sides of the mortar, so that a uniform mixture may result, which is finally passed through a well-wetted strainer of loose flannel or cheesecloth, to remove the inert woody fibre and possible impurities. In making emulsion of lycopodium, it becomes necessary to triturate the seed *dry, with some pressure*, in order to rupture the hard seed envelope; when the powder changes in color and becomes damp and adhesive from the oil, a little water is added, with which a smooth soft paste can be formed, to be further diluted by the addition of water as directed above. Emulsion of lycopodium *should never be strained*, and, if properly made, will show no particles floating on the surface; the insoluble matter which settles upon standing is readily reincorporated by agitation.

Oil emulsions, which are far more frequently used (at least in this country) than those made from seed or gum-resins, require more care in their preparation, as success depends not only on the manipulation, but also on the judicious choice of an excipient. As a general rule, it may be stated that acacia produces the whitest and most stable emulsions, because its perfect and ready solubility in water enables the operator to divide the oil quickly into minute globules, which are at once surrounded by an envelope of the mucilaginous liquid and thus kept from coalescing. The oil globules of a well-made acacia emulsion, when compared with milk under a magnifying lens, more closely resemble its fat globules than would be the case if made with other excipients. To insure success, it is essential that definite proportions of oil, gum, and water be used for making the primary emulsion, which can then be diluted with water as desired. *Not less than one-fourth nor more than one-half* as much acacia as oil should be used, and *not less than one and a half times nor more than twice as much* water as acacia. The mixing of oil, gum, and water should not be effected by the usual method of trituration, which involves pressure of the pestle against the material on the bottom and sides of the mortar, and consequent development of heat, but should be brought about by a rapid light rotary movement of the wrist, communicated to the pestle held loosely in the hand, as shown in Fig. 216; this motion partakes more of that of an egg-whip, and the oil is thus rapidly broken up into minute globules in the presence of a viscid solution.

FIG. 216.



As stated before, emulsions of fats and fixed oils are best made in a flat-bottomed mortar, three distinct methods being in use to effect the desired object, namely, a milk-like liquid, miscible with water without the separation of oil globules. By many pharmacists the method usually recommended in Great Britain is preferred; this consists in making a smooth thick mucilage of granulated acacia and water, and then adding the oil by degrees, stirring assiduously until each portion of oil is emulsified—lastly adding the water for dilution, in divided portions. The other two are sometimes called the "Continental" methods, from the fact that they are used almost exclusively in Continental Europe. They do not direct the previous solution of the gum in water, and adhere strictly to definite proportions. While the so-called "English" method yields very satisfactory results in the hands of those accustomed to it, for the inexperienced either of the other two methods is to be much preferred, such preference being based upon observation of many hundred cases in the hands of students working in the laboratories in charge of the author, who has never known of a single failure by a novice to make a perfect emulsion according to the following methods, provided, of course, that the directions as given were followed.

Place in a mortar one-fourth as much *finely powdered* acacia as the oil to be used (7.5 Gm. of acacia for 30 Cc. of oil, or ʒij for f℥j), then add the oil and triturate well together into a smooth mixture. Now add *all at once*, not gradually, twice as much water as the acacia which has been used (15 Cc. of water for 7.5 Gm. of acacia, or fʒiv for ʒij), and stir rapidly until a perfect emulsion has been formed, which is known by the appearance of a white pasty mass, free from oil particles, and a peculiar crackling noise as the pestle is drawn through the adhesive mixture. This primary emulsion should be well scraped with a spatula from the pestle and sides of the mortar, again stirred, and then the remainder of the water slowly added with constant stirring. Granulated acacia cannot be used in this method, as with so small a quantity of gum it is necessary that it dissolve almost immediately, which will not occur with the granulated variety.

The second of the so-called "Continental" methods directs increased proportions of acacia and water, by which means an equally perfect, and at the same time denser, primary emulsion is obtained. One-half as much granulated acacia as oil is used, and one and a half times as much water as gum, or one-half as much water as oil and gum together; thus, oil 30 Cc. or f℥j, granulated acacia 15 Gm. or ʒiv, and water 22.5 Cc. or fʒvj. Place the acacia in a dry mortar, add the oil and water, and stir briskly until a perfect emulsion results, which dilute with the remaining water, as in the preceding method.

If from any cause the primary emulsion should fail, it will prove a loss of time and labor to endeavor to save it by the addition of gum or water, provided the right proportions were used in the first place; the best plan is to begin over again and observe care in details. Assiduous stirring or shaking is of no avail in trying to save a "cracked" emulsion, which has a pearly appearance in the mortar, and the further addition of gum, while increasing the density of the mixture, does not always remedy the trouble.

The above methods are equally well adapted for liquid oleoresins, such as copaiba, oleoresin of cubeb, etc. If solid fats, camphor, some oleoresins and resinous extracts, as, for instance, extract of Indian cannabis, are to be administered in aqueous liquids, it will be found advantageous to dissolve them in a small quantity of fixed oil (oil of sweet almond or olive oil), and then to emulsify them in the manner directed for these oils. Salol, menthol, thymol, phosphorus, and other substances can likewise conveniently be emulsified after solution in some fixed oil. The emulsification of Peru balsam will materially be facilitated by the addition of a little alcohol or oil of sweet almond, about 10 per cent. of the volume of balsam being sufficient. If emulsions of wax or spermaceti are to be made, heat must be employed; the wax or spermaceti is melted in a mortar heated to about 65° C. (149° F.) and mixed with an equal weight of powdered acacia, after which exactly one and a half times as much water as acacia, heated to near boiling, is added, and the mixture briskly stirred. After the emulsion cools to about 30° C. (86° F.) more water may be added in small quantities, with constant stirring. Whenever double emulsions are ordered, as, for instance, a seed emulsion with that of a fixed oil, better results will be obtained if separate emulsions be made and then mixed; when castor oil is to be mixed with emulsion of almond as a vehicle, the oil should be emulsionized with the requisite quantity of acacia and water, and this primary emulsion then diluted with the almond emulsion, out of which the water necessary for the previous emulsification of the oil has been retained.

Whenever an oil emulsion is made, the rule should be observed never to measure the water in an oily graduate, as otherwise oil particles might subsequently be carried into the mixture, and, failing to be emulsified, eventually rise to the surface. The view held by some authorities, that a good emulsion is capable of emulsifying additional quantities of oil, requires modification, as pointed out by Mr. Gerrard, of England; for, although a perfect fixed-oil emulsion admits of the incorporation of more oil, this latter oil will not undergo emulsification, but simply be mixed intimately, as can be proved by the addition of water, when the newly added oil will separate. A perfect artificial emulsion should have a milk-like appearance and consistence, be miscible with water without separation, should flow readily from the mortar without leaving any adhering particles, so that it can be washed with plain water, and, if separation takes place after standing at rest for some time, a cream-like layer should rise to the surface, which can be quickly reincorporated by agitation. Heat is detrimental to the permanence of emulsions and causes separation, so also large quantities of alcohol or saline matter. Substances which have a tendency to absorb water, such as magnesia, must not be mixed with the emulsion, unless previously completely hydrated. All salts should be added in the form of solution, and, together with tinctures and other alcoholic liquids, not until the primary emulsion has been properly diluted.

Emulsions of ether, chloroform, oil of turpentine, and other volatile liquids are best prepared by agitation in a bottle after the manner first suggested by Forbes. The liquid to be emulsionized is poured into a *perfectly dry* bottle and the powdered acacia added, after which the bottle is well shaken so that the acacia may become saturated with the volatile liquid; water is then added and agitation continued until a homogeneous emulsion results, which can further be diluted by the gradual addition of water. Volatile oils and ethereal liquids will never form as perfect an emulsion as fixed oils, and separation of the mixture takes place more speedily; if care has been observed, however, in making the mixture, only a dense creamy layer will rise to the surface, which can be reincorporated by agitation. As a rule, volatile oils and ethers require more gum than fixed oils, and less than 30 grains of powdered acacia should not be used for each fluidrachm; the amount of water first added should always be equal to twice the acacia used. Oil of turpentine unites very readily with water and gum, and it is surprising to see how small a quantity of gum will suffice to form a perfect emulsion from which no oil will separate in an uncombined form, only a dense creamy layer rising, composed of the oil of turpentine, gum, and some water in intimate union; 20 grains of powdered acacia shaken in a bottle with 1 fluidounce of oil of turpentine, and 4 fluidrachms of water then added, will yield a very satisfactory emulsion, which can be kept for days without separating an oily layer. All emulsions of volatile oils are more permanent if made with the aid of some fixed oil previously added to the volatile oil; such emulsions are preferably made in a mortar.

When powdered tragacanth is preferred as an emulsifying agent, it may be used in the proportion of one-tenth or one-eighth of the necessary weight of acacia, and requires from 10 to 20 times its weight of water; it should be thoroughly mixed with the oil in the mortar or bottle, as the case may be, and after the addition of water the mixture should be stirred rapidly or shaken until the primary emulsion has been formed. The division of oil globules by means of mucilage of tragacanth is much coarser than with acacia, hence tragacanth emulsions are never so white nor seemingly so perfect; but owing to the viscosity and magma-like condition of mucilage of tragacanth the oil globules, although not finely divided, are kept from reuniting, and thus separation of an oily layer is prevented. Mixtures of tragacanth and acacia are often employed, particularly in the emulsification of cod-liver oil, to obtain greater protection against separation.

Yolk of egg has long been known as a valuable excipient in emulsions, particularly when acids or large proportions of alcoholic liquids are to be added. One yolk from an egg of average size will suffice for 1 fluidounce of a fixed oil or for ½ fluidounce of a volatile oil; in place of the simple yolk, a solution of yolk of egg 45 parts, and glycerin 55 parts, known as glyconin, may be used with advantage, 2½ fluidrachms being required for 1 fluidounce of fixed oil. In either case the oil should be added in small quantities to the yolk of egg or glyconin, previously rubbed smooth in a mortar, each portion being thoroughly incorporated before another addition is made; if the mixture should become inconveniently thick, a small quantity of water may be introduced, and after all the oil has been emulsified the prescribed amount of water is added, likewise in divided portions, with constant stirring. The readiness with which yolk of egg unites with fixed oils is due to the fact that it is itself a natural emulsion of an oil and albuminous matter. Some little care is necessary in removing the yolk of egg from the shell, to avoid contamination with the white or albumen, which has a tendency to form clots in the emulsions.

Of other emulsifying agents introduced during the last twenty years, none has been more extensively used, particularly on a large scale by manufacturers, than mucilage of Irish moss. Toward fixed oils the mucilaginous matter of Irish moss behaves somewhat like tragacanth, particularly if the solution of the former be made somewhat thick. This mucilage is made by washing the drug with cold water to remove saline and other foreign matter, then heating it with the required quantity of water in a dish, for fifteen minutes, on a boiling water-bath, and finally straining the mixture; the strength of the mucilage may be from 10 to 15 grains to the ounce, the usual strength being about 12 grains. Of the latter mucilage, 5 fluidrachms are considered sufficient for 1 fluidounce of oil, the emulsion being made by adding the oil in small portions to the mucilage contained in a bottle and agitating briskly after each addition; after all the oil has been emulsified, syrup or more water may be added as a diluent. Emulsions made with Irish moss are not so white as those made with acacia, and contain the oil in a coarser state of division; some manufacturers add acacia to the Irish moss mucilage, in order to improve the emulsion.

While milk itself is a very poor emulsifier of fats and fixed oils, its albuminoid constituent, casein, is said to be even superior to acacia. According to Leger, a French pharmacist, it is best used in the form of a saccharated powder, prepared as follows: To 4 quarts of milk warmed to 40° C. (104° F.) add 2¼ fluidounces of ammonia-water, and after setting aside for twenty-four hours withdraw the lower milk-serum from the upper fatty layer. Precipitate the casein from the milk-serum by the addition of acetic acid, and wash the precipitate by decantation with water warmed to about 40° C. (104° F.); finally collect on a wetted muslin strainer and express the moisture. Determine the amount of dry casein in the residue by heating a weighed portion to complete dryness in an air-bath; add 10 Gm. of sodium bicarbonate and sufficient sugar to obtain, when dry, a powder containing 10 per cent. of its weight of casein. The mass must be dried at a gentle heat and powdered; it keeps well for a long time in securely corked bottles. For oil emulsions, Leger recommends the making of a mucilage of 15 parts of saccharated casein with 5 parts of water, and adding to this in small portions 15 parts of oil, stirring well after each addition; finally diluting the emulsion as required.

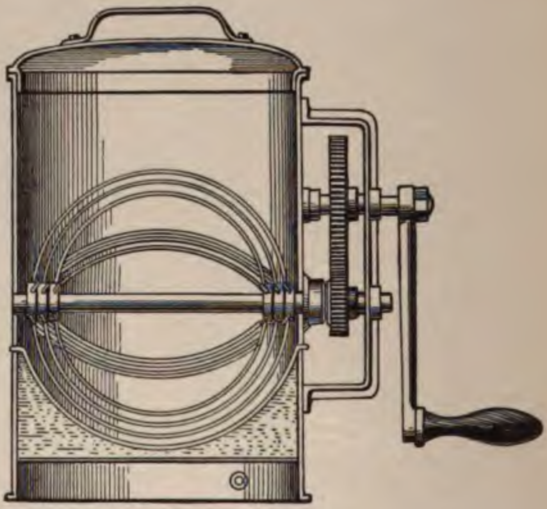
Condensed milk has also been successfully used as an emulsifying agent for castor oil and cod-liver oil. A fluidounce of the oil is mixed by trituration in a mortar, in small quantities, with ½ fluidounce of condensed milk, and, when emulsified, ½ fluidounce of water is slowly added, with constant stirring. Such emulsions, however, do not bear dilution well.

Mucilage of dextrin, made by heating 1 ounce of white dextrin with 2 ounces of water until dissolved, has been recommended as an emulsifying agent, each fluidounce of fixed oil requiring 6 fluidrachms of the mucilage, which must be cooled just short of gelatinizing, but the results are not satisfactory.

The saponaceous principles of quillaja and other drugs rich in saponins possess the property of dividing and suspending oil globules quite well if used in sufficient quantity. While the official fluidextract and tincture of quillaja could be employed for this purpose, the toxic properties of the constituents render them undesirable and they should never be used without the knowledge and consent of the physician.

For making from 1 to 5 gallons of emulsion, the apparatus known as the Morton patent egg-beater, or whisking machine, illustrated in Fig. 217, has been found very serviceable and satisfactory; it is made of heavily tinned iron, and supplied with a water-chamber underneath, by means of which either hot or cold water may be employed for tempering, whenever desired. The upper tank is provided with a rounded bottom, and the emulsification is effected by means of several heavy wire-beaters in circular form revolving rapidly in opposite directions within each other, whereby constant cross-cutting of the mixture and most perfect dashing of the constituents are insured; to prevent dust from entering, the tank is provided with a well-fitting top. The beaters are easily removed by withdrawing the frame, and the apparatus can be quickly and thoroughly cleaned.

FIG. 217.



The Morton patent egg-beater.

When emulsions are to be made on a large scale, the usual plan is to add the oil, in a thin continuous stream, to the mucilage contained in a suitable churning apparatus operated by steam power, the mixture being kept in constant agitation by rapidly revolving metallic blades frequently provided with numerous perforations. In this way 10 or 15 gallons of oil can be completely emulsified in the course of a day.

THE OFFICIAL EMULSIONS.

The Pharmacopœia recognizes 6 emulsions: 1 each made from chloroform and fixed oil, gum-resin, seed, and volatile oil with fixed oil, and 2 made from fixed oil. In each case specific directions are given for manipulation, which agree with those explained elsewhere.

ALPHABETICAL LIST OF THE OFFICIAL EMULSIONS.

Latin Name.	English Name.	Composition.
Emulsum Amygdalæ (Mistura Amygdalæ)	Emulsion of Almond	Sweet Almond 60 Gm., Acacia 10 Gm., Sugar 30 Gm., Water sufficient to make 1000 Cc.
Emulsum Asafœtidæ (Mistura Asafœtidæ)	Emulsion of Asafetida	Asafetida 40 Gm., Water sufficient to make 1000 Cc.
Emulsum Chloroformi (Mistura Chloroformi)	Emulsion of Chloroform	Chloroform 40 Cc., Expressed Oil of Almond 60 Cc., Tragacanth 10 Gm., Water sufficient to make 1000 Cc.
Emulsum Olei Morrhuæ	Emulsion of Cod-liver Oil	Cod-liver Oil 500 Cc., Acacia 125 Gm., Syrup 100 Cc., Oil of Gaultheria 4 Cc., Water sufficient to make 1000 Cc.
Emulsum Olei Morrhuæ cum Hypophosphitibus	Emulsion of Cod-liver Oil with Hypophosphites	Cod-liver Oil 500 Cc., Acacia 125 Gm., Syrup 100 Cc., Oil of Gaultheria 4 Cc., Calcium Hypophosphite 10 Gm., Potassium Hypophosphite 5 Gm., Sodium Hypophosphite 5 Gm., Water sufficient to make 1000 Cc.
Emulsum Olei Terebinthinæ	Emulsion of Oil of Turpentine	Rectified Oil of Turpentine 15 Cc., Expressed Oil of Almond 5 Cc., Syrup 25 Cc., Acacia 15 Gm., Water sufficient to make 100 Cc.

Special Remarks.

Emulsion of Almond.—The Pharmacopœia directs the almond, acacia, and sugar to be thoroughly mixed and then incorporated with the water. This is best done by first making a smooth paste with a small quantity of water, and then gradually diluting with the remainder of the water, so that a uniform liquid may result.

The acacia and sugar prescribed in the official formula are by no means essential to the formation of a perfect emulsion, although they add to the stability of the preparation. Emulsion of almond more closely resembles cows' milk in appearance than any other seed or oil emulsion made; the fixed oil present is kept suspended in a very fine state of division by means of the albuminous matter known as emulsin or synaptase, which constitutes the chief body of the seed. Blanched almonds should always be used, so that a pure white liquid may result. Almonds are best blanched by macerating them in warm water until the skin becomes loose, when it can be quickly removed by simple pressure between the fingers. Emulsion of almond is also known as *milk of almond*, and should always be made fresh when wanted. When intended as a solvent or vehicle for local applications, such as mercuric chloride, borax, zinc oxide, etc., it must invariably be made without the sugar and acacia directed in the official formula.

Emulsion of Asafetida.—As already stated on page 316, only select tears of the gum-resin should be used for this emulsion. These are crushed into a moderately coarse powder and beaten into a perfectly smooth paste with a very small quantity of water, after which more water is gradually added, so as to enable the operator to produce a perfectly homogeneous mixture. In order to accomplish this it is necessary that the paste first obtained be scraped from the pestle and sides of the mortar and gradually reduced to a syrupy consistence by the use of small quantities of water. After straining the finished product through a previously moistened piece of flannel, only extraneous matter, such as sand, woody fibre, etc., should be left behind, but no particles of the gum-resin. Emulsion of asafetida is also known as milk of asafetida, and is sometimes prescribed by physicians as lac asafœtidæ. The color of the emulsion is usually white, but may be yellowish, pink, or even reddish, dependent upon coloring-matter unavoidably present in the gum-resin.

The other official emulsions do not require special comment, except to state that in the case of both the Emulsion of Chloroform and the Emulsion of Oil of Turpentine the preparation is rendered more stable by the addition of the fixed oil. If the official directions for preparing the emulsions are strictly followed, satisfactory products will be obtained in every instance. Whenever solutions of salts are to be mixed with emulsions, as in the case of the official Emulsion of Cod-liver Oil with Hypophospites, they should be added after the primary emulsion has been properly diluted. The same precaution applies to the addition of syrups and tinctures.

CHAPTER XXVII.

MIXTURES.

THE term "mixture" in pharmacy, and more particularly in dispensing operations, is applied to liquid medicines which either contain insoluble substances in suspension or are composed of two or more liquids, with or without the addition of saline or other material in solution; in its more restricted application the term is applied to such medicines as are intended for internal administration. In only a few cases, in which the stability of the preparation for a considerable length of time can reasonably be assured, are mixtures kept in stock; hence the extemporaneous preparation of mixtures is a matter of constant occurrence, as it is with physicians a favorite method of administering medicines, because more extended use can be made of excipients and flavoring agents, with a view of improving the mixture pharmaceutically and therapeutically. Considerable skill and judgment are frequently necessary in the preparation of mixtures, so that the object of the prescriber may be fully attained and each fraction of the mixture contain an aliquot part of all the ingredients. All insoluble or only partly soluble substances, particularly those of a vegetable nature, should be brought to the condition of smooth and uniform suspension by trituration in the form of very fine powder with the liquid in the mortar; this is best done by first rubbing into a smooth paste with a portion of the liquid and then diluting this with the remainder, constantly stirring. Calcined magnesia or magnesia and charcoal can best be brought into a uniform mixture with water, by stirring at once with sufficient water to overcome the tendency of the magnesia to "set" in a gelatinous mass; a *small* quantity of water added to calcined magnesia also causes it to become gritty and difficult to mix. Some prefer to add the magnesia to the water and diffuse by agitation. In all cases the mixture should be passed through a loosely textured cloth. All powerful remedies, such as mercuric chloride, arsenous acid, the salts of morphine, strychnine, etc., should always be brought to a state of perfect solution before they are added to the other ingredients of a mixture, so as to insure a uniform distribution throughout the liquid. Substances which are readily diffusible in the liquid by agitation of the bottle do not, as a rule, require the addition of an excipient to insure their uniform suspension; but other insoluble substances which are relatively much heavier than water, or are inclined to float on the surface of the liquid, demand the addition of some mucilaginous or other body to increase the density. Syrup, glycerin, or honey is frequently preferable to acacia or tragacanth, especially in the case of heavy metallic salts, liable to form, with the gum, a compact mass, which cannot be readily suspended by agitation.

Formerly emulsions were recognized among the mixtures, but they are now considered as a distinct class of preparations, the characteristics of which have been described in the preceding chapter.

In connection with the preparation of mixtures, it becomes necessary to consider the subject of incompatibility; this term is applied to the antagonism or disability of harmonious coexistence, which is exhibited by numerous substances when brought into contact with certain other substances. Liquids which are not mutually intersoluble, although they can be brought into homogeneous mixture with the aid of excipients, are often said to be incompatible with each other, as in the case of fixed oils and water, chloroform and glycerin, etc.; but, strictly speaking, the term incompatibility in pharmacy refers to the relation existing between two or more bodies by reason of which they cannot be mixed without undergoing or producing some change of a physical or chemical nature. Three kinds of incompatibility exist—pharmaceutical, chemical, and therapeutic—of which the pharmacist must take note, and for the proper understanding of which he must rely upon his knowledge of the physical, chemical, and medical properties of drugs.

Pharmaceutical incompatibility is such as affects the physical properties of substances, and is chiefly confined to their solubility; it may result in the partial or total separation of matter held in solution, which may include valuable constituents of the mixture, or it may cause simply a separation of liquids from each other. The changes due to pharmaceutical incompatibility, being entirely of a physical character, can often be avoided or overcome by judicious manipulation or by the addition of some suitable excipient or protective agent. The mixture of strongly alcoholic liquids with solutions of acacia—of acid or neutral aqueous liquids with resinous tinctures—of alcoholic or ethereal solutions of volatile oils and other substances with aqueous liquids—the admixture of solids which undergo liquefaction by reason of intersolubility, as in the case of camphor with solid fats, hydrated chloral, thymol, salol, menthol, etc.—the addition of certain metallic salts to vegetable solutions, causing gelatinization, as in the case of tincture of ferric chloride and mucilage of acacia—are all instances of pharmaceutical incompatibilities. In many cases of physical incompatibility the trouble may be averted by appropriate dilution before mixing, as, for instance, when spirit of nitrous ether or tincture of ferric chloride is to be mixed with a strong mucilage of acacia: a perfectly uniform mixture, free from precipitate or gelatinization, can be prepared if the mucilage as well as the spirit or tincture be first largely diluted with water, and such should be the invariable rule when these substances are prescribed together. When tinctures of asafetida, guaiac, lupulin, myrrh, and similar substances are ordered in combination with aqueous saline liquids, separation of the resinous matter will invariably result unless a protective agent is present, by means of which the finely divided precipitate is kept in perfect suspension.

The value of honey as a preventive of unsightly precipitation may be exemplified in the following well-known prescription, which has caused some pharmacists much annoyance :

℞—Potassii Chloratis	ʒj.
Tinct. Guaiaci Tinct. Cinchonæ Co. Mellis	āā ℥ss.
Aquæ	q. s. ad ℥iij.—M.

If the honey be put into a mortar and the tincture of guaiac slowly added so that the two become well mixed, no separation of resinous matter will occur if the potassium chlorate dissolved in 1½ fluidounces of water be added with constant stirring; the compound tincture of cinchona is added lastly, and a uniform mixture of pink color results. If, on the other hand, the honey be mixed with the solution of potassium chlorate and a mixture of the two tinctures then added, trouble is sure to arise, as also if the honey be mixed with the two tinctures in a bottle and the solution of potassium chlorate then added.

Syrups, honey, and glycerin are frequently associated with resinous tinctures by physicians, for the purpose of avoiding the separation of resin, and, if used in sufficient quantity, will answer the purpose; in the absence, however, of such provision, it is the duty of the pharmacist to add some inert substance which will enable him to prepare a mixture of uniform composition. If the following two prescriptions be dispensed exactly as ordered, the resin of the tincture in both cases would be precipitated and gradually deposited on the sides and bottom of the bottle, thus depriving the patient of an important part of the medicine; no amount of shaking will even temporarily suspend the precipitated resin uniformly, but only increase its separation from the liquid.

℞—Potassii Bromidi	ʒiv.
Tinct. Lupulini	℥j.
Aquæ Menthæ Vir.	℥ij.—M.

℞—Potassii Chloratis	ʒij.
Tinct. Guaiaci	℥j.
Aquæ	q. s. ad ℥iv.—M.

By mixing the resinous tincture or fluid extract with powdered tragacanth in a mortar, and then adding the water or saline solution gradually, with constant stirring, a perfect mixture can be obtained from which the suspended resin separates very slowly in a finely divided form, so as to be readily reincorporated by simple agitation. The proportion of tragacanth to be used will depend, to some extent, upon the volume of dilution; for instance, in the above prescriptions, 10 or 12 grains will be amply sufficient, while if a 6 oz. mixture were intended, 15 or 18 grains would be preferable. As a rule, 10 grains of tragacanth will be required for each fluidounce of a tincture or half fluidounce of a fluid extract.

This general rule to suspend the precipitated resinous matter by means of tragacanth should not be adhered to, however, in all cases, as, for instance, when a cosmetic lotion containing tincture of benzoin, glycerin, and water, is desired, or in the case of a mouth-wash composed of tincture of myrrh and water. In both mixtures the presence of tragacanth would prove decidedly objectionable, and very satisfactory results can be obtained by pouring the respective tincture slowly and in a thin stream into cold water contained in a bottle, adding any glycerin that may have been ordered, and mixing the ingredients by repeatedly and slowly inverting the bottle. The resinous matter in such cases is precipitated in a finely divided form and remains well suspended in the fluid. Strong agitation would cause rapid separation in lumps.

Other cases of physical incompatibility may be observed when strong solutions of metallic salts are to be made with aromatic waters; for instance, potassium or sodium bromide with camphor-water or peppermint-water, etc. Part of the camphor or oil of peppermint will be precipitated, and a remedy for the trouble may be found either in the use of plain distilled water or in the addition of a small quantity of alcohol for a corresponding amount of the medicated water, but such changes should not be made without consulting the prescriber. A solution of potassium bromide ℥j and camphor water ℥iv will require ʒiiss–ʒiij of alcohol, which is preferably added to sufficient camphor water to make a volume of 4 fluidounces, before dissolving the potassium salt.

The turbidity caused by the partial separation of volatile oil or other bodies when an alcoholic solution of the same is added to aqueous fluids is due to the decreased solubility of the substance in the diluted spirit, and cannot be overcome by the ordinary methods; filtration with the aid of such media as purified talcum, calcium phosphate, etc., is not always permissible, and then the application of the general rule—*never to dispense a mixture containing insoluble matter without a "Shake well before using" label*—is all that can be done by the pharmacist.

Sometimes the particular order of mixing two or more liquids will have a marked effect on the appearance of the finished product. Thus, in the preparation of the official aromatic spirit of ammonia, if the aqueous solution of ammonium carbonate be added to the alcoholic solution of the oils, as directed in the Pharmacopœia, a saline precipitate will almost invariably form, which subsequently is redissolved very slowly, often requiring days to produce a clear liquid. If, however, the alcoholic solution of the oils be added slowly to the watery alkaline solution, no precipitation whatever occurs.

Chemical incompatibility, as its name indicates, depends upon the chemical properties of substances, and invariably involves decomposition of one or all of the bodies brought into contact, with the resulting formation of new compounds. The existence of chemical incompatibility has proved most valuable in the study of inorganic and organic matter, and forms the basis upon which rests the very extensive superstructure of analytical chemistry. Chemical decomposition is not always accompanied by the separation of insoluble matter, for in numerous cases the newly formed compound is perfectly soluble in the liquid present. Among the most dangerous incompatibles are mixtures of the chlorates or permanganates with readily oxidizable substances; hence particular care must be exercised in bringing the former into intimate contact with organic matter, so as to avoid possible serious explosions.

There are different conditions under which chemical incompatibility manifests itself, chief among which are the following:

1. Two salts composed of different acid and basic radicals, when brought together in a state of solution, mutually decompose each other; the resulting new compounds may both remain in solution, in which case no evidence of decomposition is apparent, and it scarcely seems proper to consider the two salts used as incompatible with each other, as when solutions of ammonium chloride and potassium iodide are mixed, or those of cupric sulphate and zinc acetate. When, however, one of the new compounds is insoluble in the liquid and is deposited as a precipitate, true incompatibility has been established; as in the case of a mixture of solutions of lead nitrate and potassium iodide, lead iodide being precipitated. Sometimes the new insoluble compound enters into union and solution with one of the original substances, if the latter is present in excess, in which case the chemical incompatibility of the original two substances remains, and the resolution of the insoluble compound must be looked upon as a new operation. Such examples are presented by mercuric chloride and potassium iodide, if either salt is in excess, or by potassium cyanide and silver nitrate, the former salt being in excess.

2. Salts of the heavy metals, and, in many instances, also those of the alkaline earths and earths, are decomposed by the alkalies or their carbonates, forming insoluble compounds; hence incompatibility exists between such salts. As examples may be mentioned mercuric chloride with potassium hydroxide, lime-water with sodium bicarbonate, calcium chloride with potassium carbonate, and alum with sodium carbonate.

Bismuth subnitrate is frequently prescribed in a mixture with sodium bicarbonate, and almost invariably decomposition takes place, resulting in a more or less violent disengagement of carbon dioxide; as the reaction takes place slowly, at times it may not occur until the mixture has been transferred to a bottle and corked. The remedy lies either in using the bismuth subcarbonate in place of the subnitrate, or in mixing the subnitrate and bicarbonate in a mortar and adding a little boiling water, so as to hasten and complete the reaction.

3. When oxidizing agents are brought into direct contact with organic matter chemical reaction at once ensues, which is often of a violent nature, and is among the most important incompatibilities met with. To this class belong the trituration of potassium chlorate with sulphur, sugar, tannin, or acacia; the solution of chromic acid or potassium permanganate with glycerin, etc.

4. The association of the salts of gold and silver with organic substances and other reducing agents gives rise to an exhibition of incompatibility by converting the gold and silver to the metallic state, thereby rendering them less soluble, as, for instance, when silver nitrate is dissolved in rose-water instead of plain distilled water. All organic matter has a decomposing effect upon the compounds of gold and silver, but more particularly glucose, honey, syrup, and glycerin; hence these should be avoided in prescriptions.

5. Salts when brought in contact, either in the dry state or in solution, with acids or bases stronger than their own acid or basic radicals, will suffer decomposition, the result being new compounds, with the evolution of the old acid or base, as in the preparation of the official solution of ammonium acetate. The decomposition of salts by stronger acids or bases is frequently resorted to intentionally, as in the well-known "Neutral Mixture," made from lemon-juice and potassium bicarbonate, and in "Preston or Smelling Salts," composed of ammonium chloride and lime, usually flavored with oil of lemon and oil of lavender. In the former case it is desired to keep a large portion of the eliminated carbonic acid in solution, while in the latter the gradually freed ammonia gas is the chief object sought.

Whenever carbonates are prescribed with an acid liquid the dispenser should allow the reaction to be completed before corking the vial, so that the greater portion of the gas may escape, and caution the patient to keep the vial in a cool place and not violently agitate it. If a viscid or saponaceous liquid is also to be added, as mucilage or syrup of senega, it is all the more important that chemical reaction be allowed to subside before the addition is made, and that as little carbon dioxide as possible be kept in the solution.

With some physicians, the following is a favorite prescription:

℞—Ammonii Carbonatis Ammonii Chloridi	āā ʒj.
Syrupi Scillæ Syrupi Senegæ	āā ℥j.
Syrupi Tolutani	℥ij.
Ft. sol.	

The proper way of mixing these ingredients is to rub the salts to a fine powder, and add to them, *while in the mortar*, the syrups of squill and tolu previously mixed, stirring the mixture with the pestle *until effervescence ceases;* finally add the syrup of senega. If a persistent froth forms on the surface of the liquid, this may be quickly dispelled by carefully sprinkling a few drops of alcohol over it before the mixture is transferred to a bottle.

To this class of incompatibilities belong also the decomposition and precipitation caused in fluidextract of licorice by acids; the sweet principle in licorice is ammonium glycyrrhizate, which, upon addition of dilute sulphuric or other acid, is decomposed, glycyrrhizin being deposited on the sides and bottom of the vessel. Physicians sometimes prescribe an acid solution of quinine together with fluidextract of licorice, in the hope of disguising the bitter taste, overlooking the fact that the bitter taste of quinine is always intensified by bringing the latter into solution. As the intended effect of the licorice is defeated by the presence of an acid, there is but one course open to the pharmacist with prescriptions of this kind, namely, to omit the acid, triturate the quinine with the fluidextract or syrup of licorice, and dispense the mixture with a "Shake well before using" label. It is advisable at the same time to explain to the physician what has been done, giving the reason therefor, so as to avoid, if possible, a repetition of the blunder.

6. The salts of the alkaloids are decomposed by certain salts of the alkalies, with the production of insoluble or sparingly soluble compounds; therefore such combinations require the special attention of pharmacists in order to guard against accidents. As a rule, the alkali carbonates, iodides, and bromides are incompatible with alkaloidal salts, while the sulphates, nitrates, and chlorides appear to cause no trouble; hence in the case of the first-named salts the directions to shake the mixture should always be put on the bottle. The presence of a certain amount of alcohol in the liquid will prevent the precipitation of the newly formed alkaloidal salt, as may be demonstrated in the following prescription:

℞—Strychninæ Sulphatis	gr. j.
Potassii Bromidi	ʒj.
Aquæ destillatæ	q. s. ad ℥iv.
Ft. sol.	

If the solution be prepared as written, strychnine bromide will gradually be deposited in colorless crystals, and may cause serious results should the same be retained in the bottle and a large quantity be taken with the last dose or two. If, however, equal volumes of aromatic elixir and water be used in place of water alone, no separation of strychnine bromide will occur. At least 12 per cent. of alcohol must be present in the solution to prevent precipitation.

In a few rare cases, when a sufficient quantity of solvent is present to take up the alkaloid in its pure state, it may be preferable to use the latter in place of its salt, as, for instance, in the following prescription:

℞—Codeinæ Sulphatis	gr. viij.
Potassii Bromidi	℥j.
Aquæ destillatæ	q. s. ut ft. ʒiv.

Ft. sol.

It was found that if the codeine sulphate was used, as prescribed, a precipitate invariably formed, which was with difficulty uniformly suspended by agitation, but by using the pure alkaloid codeine in place of the salt a permanently clear solution was obtained. Morphine sulphate is sometimes prescribed in conjunction with sodium bicarbonate, the result being a minutely crystalline precipitate. Quinine sulphate and potassium acetate should not be associated in solution, on account of the slight solubility of the quinine acetate, which is formed as a very bulky precipitate, and may cause solidification of the mixture.

7. Vegetable astringents are incompatible with alkaloids, glucosides, albumen, gelatin, and many metallic salts; in some cases curdy precipitates are formed, which afterward adhere to the sides of the vessels, while in other cases light, readily diffusible precipitates are obtained, or possibly only turbidity or discoloration ensues. The character of such a mixture depends to some extent upon the degree of dilution and the presence of other bodies. Quinine and tannin are sometimes prescribed together, but should never be triturated with water, as a tough, insoluble mass would at once be formed; the two substances are best mixed with syrup and afterward diluted with water, if desired, when the insoluble quinine tannate can be readily suspended by simple agitation. The formation of ink depends upon the incompatibility of tannin with iron salts, and is a fruitful source of annoyance to the pharmacist. The value of strong coffee and tea or similar astringent infusions as antidotes for metallic poisoning is due to the formation of sparingly soluble compounds. Vegetable astringents have been found incompatible also with spirit of nitrous ether, several explosions have occurred from mixing the latter with the fluidextracts of uva ursi, matico, geranium, and even gentian; the gas liberated by these reactions appeared heavily charged with some nitrous compound.

Spirit of nitrous ether unless free from acidity, which is rarely the case except in the freshly made article, is incompatible with solutions of alkali iodides and bromides, causing the liberation of iodine and bromine, respectively, as shown by the high color of the liquid. With solutions of antipyrine it gives rise to the formation of a green-colored compound, known as isonitroso-antipyrine, which, however, is not poisonous, as was formerly believed. Whenever spirit of nitrous ether, therefore, is to be dispensed in such mixtures, it should be first carefully neutralized with sodium or potassium bicarbonate; this will, however, not prevent the development of acid for all times, as the spirit of nitrous ether will gradually undergo decomposition in the presence of water.

The presence of certain protective agents has been known to avert, or at least to modify, chemical decomposition between some substances; in such cases it is, of course, essential that the protective agent be mixed with one of the substances before the other is added. The following examples will show the action of glycerin, acacia, and syrup, in this respect. Physicians frequently prescribe cocaine hydrochloride or morphine salts in solution, together with borax, which causes precipitation and thus unfits the solution for use; the addition of a little glycerin prevents the decomposition. Zinc chloride and borax, prescribed together in solution, will cause the formation of insoluble zinc borate, which is prevented, however, by the presence of glycerin; strange to say, such a clear solution containing glycerin will bear further dilution with water only up to a certain point, beyond which precipitation ensues. The action of the glycerin in the foregoing cases is not clearly understood, but, reasoning from the effect of glycerin on borax alone, it may be assumed that a similar action obtains in the mixture with alkaloidal and other salts, the glycerin decomposing the borax by liberating a part of the boric acid, which itself is perfectly compatible with the salts above mentioned, as has been shown by making the solutions with boric acid, instead of borax or borax and glycerin. On the other hand, glycerin may sometimes act as a disturbing agent and cause decomposition which otherwise would not occur. Borax and sodium bicarbonate are perfectly compatible in aqueous solution, and are frequently prescribed together; if glycerin be present, reaction is set up by the boric acid liberated from the borax, and the sodium bicarbonate is decomposed with copious evolution of carbon dioxide. Such a mixture must be made in a mortar and the reaction allowed to subside before bottling it.

Corrosive mercuric chloride and lime-water are known to be incompatible, but are often ordered together, with the view of utilizing the freshly formed yellow mercuric oxide in moist condition; mercuric chloride will also precipitate acacia from a strong solution, but if a dilute solution of mercuric chloride be added to mucilage of acacia and subsequently mixed with lime-water, no precipitate whatever will occur for several days, when finally a grayish deposit of finely divided metallic mercury or mercurous oxide is formed. When a physician orders such a combination as mercuric chloride, water, mucilage of acacia, and lime-water, the object is plainly to keep the mercuric oxide better suspended, and the mixture should be made by adding the mucilage last of all, after decomposition of the mercuric chloride has been completed.

Chemical incompatibility may result in rendering a mixture less active, or even inert, from the formation of insoluble compounds, as when tartar emetic is ordered in combination with syrup of wild cherry, or tincture of digitalis with tincture of cinnamon, etc.; on the other hand, the medicinal activity of the mixture may be intensified by the formation of poisonous compounds, as in the case of mercurous iodide with soluble iodides, producing mercuric iodide and metallic mercury, or the association of calomel with soluble chlorides or iodides, etc. In all such cases the pharmacist should consult the prescriber and acquaint him with the prospective results.

A well-marked case of double incompatibility, both physical and chemical, is exhibited in the following prescription :

℞—Zinci Sulphatis	0.650	Gm.
Mucilaginis Acaciæ	30.0	Cc.
Aquæ destillatæ	90.0	Cc.
Liq. Plumbi Subacetatis	4.0	Cc.—M.

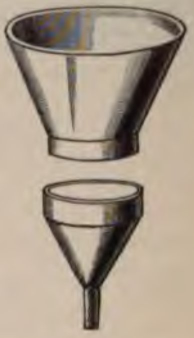
It is very evident that decomposition between the zinc and lead salts is desired, but the incompatibility existing between the mucilage of acacia and solution of lead subacetate must be overcome, and this can be done effectually by following a certain order of mixing. The zinc sulphate should be dissolved in the water and the solution of lead subacetate then added, which will cause a precipitate of lead sulphate to form ; to this mixture the mucilage of acacia is added and the whole shaken—no precipitation of gum will occur, and the newly formed lead salt will remain well suspended.

It must not be supposed, however, that because precipitation occurs as a result of chemical incompatibility the mixture is always rendered inert thereby ; the decomposition is often intentional with a view to obtaining the insoluble compound in a freshly formed and more active condition. Such instances are found in the well-known "black wash" and "yellow wash" (prepared from lime water with calomel and corrosive sublimate, respectively), in the mixture of solutions of tannin and of lead subacetate, which produce a magma-like precipitate of lead tannate, and in the frequently prescribed mixture of zinc sulphate with a solution of lead acetate, giving the freshly precipitated lead sulphate, which is much preferred. The official compound iron mixture is another instance of intentional decomposition, the newly formed ferrous carbonate being the object sought. It requires no little judgment on the part of the pharmacist to discern when the prescriber intentionally orders chemically incompatible substances together, or when this happens from a want of familiarity with chemical reactions.

Therapeutic incompatibility depends entirely upon the antagonism existing between drugs in regard to their physiological effect or medical action, and does not properly belong to the domain of pharmacy; the remedy for such a condition lies solely in the hands of the physician, who is supposed to be familiar with the requirements of his patients and the therapeutic action of drugs. Sometimes the intended medicinal effect of a substance is destroyed by chemical action, as when ammonium carbonate is asociated with syrup of squill; this, however, cannot be considered as a therapeutic incompatibility.

While it is well understood in prescription practice that solutions should always be filtered through a pledget of cotton placed in the throat of a funnel to remove motes and specks, the rule should also prevail in dispensing mixtures that the mixture be strained through moderately coarse bolting-cloth, in order that the insoluble matter be free from lumps and in a uniformly divided state; the straining is best accomplished by placing the bolting-cloth between the upper and lower parts of a rubber or tin funnel, as shown in Fig. 218, which can be inserted directly into the prescription vial.

FIG. 218.



The subject of incompatibility is practically an endless one, and the reader is referred for further detailed information to two books that should be in every pharmacist's library, namely, Ruddiman's *Incompatibilities in Prescriptions* and Scoville's *Art of Compounding*. The following summary will, to some extent, aid the dispenser in determining the character of numerous mixtures; it must be borne in mind, however, as stated before, that not all incompatibles produce inert or poisonous compounds, and that while in many cases the incompatibility can be overcome by appropriate means, physicians frequently associate incompatible substances for a specific purpose.

SUMMARY OF INCOMPATIBILITIES. (After HAGER.)

Acacia	with	ferric chloride, alcohol, borax, lead salts, and ethereal tinctures.
Acids in general	"	alkalies, alkaline fluids, acetates, and metallic oxides.
Acid, Arsenous	"	lime-water, magnesia, and oxides of iron.
Acid, Carbolic	"	potassium permanganate, iodine, bromine, caustic alkalies, and iron salts.
Acid, Chromic	"	glycerin, alcohol, ether, essential oils, and organic matter in general.
Acid, Picric	"	alkaloidal salts, dry acids, iodine, sulphur, and organic salts. (These incompatibilities extend also to the salts of picric acid.)
Acid, Salicylic	"	potassium permanganate, iron salts, lime-water, potassium iodide, and soap. (These incompatibilities extend also to the salts of salicylic acid.) Alkali salicylates will darken unless an excess of acid be present.
Acid, Tannic	"	mucilages, tartar emetic, silver nitrate, metallic salts in general, alkaloids and their salts, lime-water, potassium chlorate, alkali carbonates and bicarbonates, albumen, gelatin, and chlorine water.
Albumen	"	mineral acids, alcohol, mercuric chloride, and vegetable astringents.
Alkaloidal Salts	"	borax, tannin, and all vegetable astringents, alkali carbonates, the permanganates, iodides, liquorice, strong mucilages, magnesium carbonate, and alkaline tinctures.
Alum	"	alkalies and alkali carbonates.

Ammonium Acetate Ammonium Bromide	with mineral acids, alkali carbonates, chlorine, potassium chlorate and dichromate, silver nitrate, mercurous chloride and nitrate.
Ammonium Chloride Ammonium Phosphate	" carbonates of the alkalies and earths.
Amyl Nitrite	" alcohol, tinctures in general, alkali carbonates, calomel, lead salts, potassium iodide, the bromides and ferrous salts.
Antimony, Sulphurated	" sodium bicarbonate, potassium bitartrate, bismuth subnitrate and calomel.
Antipyrine	" sodium salicylate (dry), calomel, chloral hydrate, and spirit of nitrous ether if acid.
Apomorphine Hydrochloride	" sodium carbonate and bicarbonate, iodine, tannin, and iron salts.
Barium Chloride	" sulphuric and phosphoric acids and their salts, carbonates, tartrates, vegetable infusions and medicinal wines.
Bismuth Subnitrate	" calomel, tannin, sulphur, and antimony sulphide.
Calcium Chloride	" calomel, sulphates, phosphates, tartrates and carbonates.
Calcium Hypophosphite	" potassium chlorate, iodide, and permanganate; also chlorinated lime (These incompatibilities extend to all hypophosphites.)
Calomel (Mercurous Chloride)	" acids, acid salts, alkali carbonates, lime-water, ammonium chloride, iodine, potassium iodide, ferrous chloride and iodide, sulphur, bitter-almond water, cherry-laurel water, antimony sulphide, and antipyrine.
Chloral Hydrate	" water (slow decomposition), warm water, alkali carbonates and organic salts, calomel, potassium cyanide, antipyrine, salts of ammonium, mercurous nitrate, permanganates, alcohol, tinctures in general, bromides and iodides.
Chlorine Water	" alkalies and their carbonates, ammonium salts, salts of the organic acids, lead salts, silver nitrate, mucilages, tannin, extracts, tinctures, infusions, emulsions and milk.
Corrosive Sublimate (Mercuric Chloride)	" lime-water, soap, iodine, opium, potassium iodide, organic acids, tannin, and alkali carbonates.
Digitalis	" tannin, lead acetate, iodine, potassium iodide, iron salts, and alkali carbonates.
Iodine	" ammonia, starch, metallic salts, fatty and volatile oils, emulsions, carbolic acid, chloral hydrate, acacia, tragacanth, magnesium carbonate, and sodium thiosulphate (hyposulphite).
Iodoform	" silver and other nitrates, potassium chlorate, nitrites, and mineral acids. (The modification or destruction of the odor of iodoform by the following substances points to incompatibility: tannin, Peru balsam, tincture of myrrh, naphtalene, cumarin, and the volatile oils of anise, bergamot, fennel, peppermint and turpentine.)
Iron, Reduced	" aloes, tannin, infusions, extracts, metallic and alkaloidal salts.
Iron Salts	" alkali carbonates and bicarbonates, mucilages, tannin, infusions, extracts and astringent tinctures.

Lead Acetate (also Lead Subacetate)	with	opium, lime-water, ammonium chloride, alum, potassium iodide, iodine, acacia, tragacanth, tannin, carbonates and sulphates, and sulphuric and hydrochloric acids. (Normal lead acetate is compatible with mucilage of acacia, but the basic or subacetate causes precipitates, even in minute quantities.)
Lime, Chlorinated	"	ammonium chloride, sulphur, tannin, metallic sulphides, glycerin, volatile oils and fatty substances.
Lime Water	"	acids, ammonium salts, carbonates, tartrates, metallic salts, tannin, infusions and many tinctures.
Morphine Salts	"	the salts of iron, manganese and silver, potassium chlorate and permanganate, nitrites and nitrates, carbonates of the alkalies and the earths, amyl nitrite and bitter-almond water.
Musk	"	acids, acetates, tannin, ergot and metallic salts.
Opium, including the Tincture and Extract of Opium	"	alkali carbonates, tannin, metallic salts, iodine, chlorine-water, and the preparations of nux vomica and belladonna.
Pepsin	"	alkaline substances, alcohol and tinctures in general.
Potassium Bromide	"	mineral acids, chlorine-water, and the salts of mercury and silver.
Potassium Chlorate	"	mineral acids, tannin, catechu, sulphur, charcoal, calomel, sulphites, ferrous salts, nitrites, hypophosphites, sugar, honey and vegetable powders.
Potassium Iodide	"	acids and acid salts, alkaloidal salts, silver nitrate, ferric salts, potassium chlorate, spirit of nitrous ether (if acid) and salts of lead and mercury.
Potassium Permanganate	"	fatty and volatile oils, alcohol, glycerin, ammonia and ammonium salts, alkaloids, sulphur, charcoal and organic substances in general.
Silver Nitrate	"	hydrochloric, sulphuric, acetic, and tartaric acids and their salts, hydrocyanic acid, iodine, potassium iodide and bromide, antimony, carbonates of the earths and astringent tinctures.
Sodium Bicarbonate	"	acids and acid salts, tannin, metallic and alkaloidal salts.
Tartar Emetic	"	acids and alkalies, calomel, tannin, soap, acacia, opium and vegetable astringents.

In Europe, effervescing mixtures are often prescribed under the name "Saturations," which are made by adding to lemon-juice, vinegar, or tartaric or citric acid solution, sufficient of an alkali carbonate to produce a neutral or nearly neutral salt, the liquid retaining in solution a large portion of the carbon dioxide evolved, which adds materially to the refreshing taste of the mixture. In the Pharmacopœia will be found a complete table of the quantity of different alkalies and alkali carbonates necessary to neutralize 100 parts of the various official acids.

THE OFFICIAL MIXTURES.

Of the 4 preparations recognized as mixtures in the Pharmacopœia, only 2 are fit to be kept on hand for several days or longer in warm weather; the other 2 should be freshly made when needed, owing to their rapid deterioration.

TABLE OF THE OFFICIAL MIXTURES.

Latin Name.	English Name.	Proportion of Ingredients.
Mistura Cretæ . . .	Chalk Mixture . .	Comp. Chalk Powder 200 Gm., Cinnamon-water 400 Cc., Water sufficient to make 1000 Cc.
Mistura Ferri Composita	Compound Iron Mixture (Griffith's Mixture) .	Ferrous Sulphate in crystals 6 Gm., Myrrh 18 Gm., Sugar 18 Gm., Potassium Carbonate 8 Gm., Spirit of Lavender 60 Cc., Rose Water sufficient to make 1000 Cc.
Mistura Glycyrrhizæ Composita	Compound Mixture of Glycyrrhiza (Brown Mixture)	Pure Extract of Glycyrrhiza 30 Gm., Granulated Acacia 30 Gm., Syrup 50 Cc., Camphorated Tincture of Opium 120 Cc., Wine of Antimony 60 Cc., Spirit of Nitrous Ether 30 Cc., Water sufficient to make 1000 Cc.
Mistura Rhei et Sodæ	Mixture of Rhubarb and Soda .	Sodium Bicarbonate 35 Gm., Fluidextract of Rhubarb 15 Cc., Fluidextract of Ipecac 3 Cc., Glycerin 350 Cc., Spirit of Peppermint 35 Cc., Water sufficient to make 1000 Cc.

Special Remarks.

Chalk Mixture.—The compound chalk powder directed for this preparation is the official powder composed of 3 parts of prepared chalk, 2 parts of acacia, and 5 parts of sugar, the insoluble chalk being kept in suspension by the gum and sugar in solution. Precipitated calcium carbonate must not be used in making this mixture, as it is crystalline and does not make so smooth a preparation, nor remain so perfectly in suspension as the prepared chalk. Chalk mixture should be made in small quantities and kept in a cold place.

Compound Iron Mixture.—The preparation of this mixture presents no difficulty if good tears of myrrh be selected and the directions strictly followed. The first step is to triturate the myrrh, sugar, and potassium carbonate with 700 Cc. of rose water, gradually added so that a uniform emulsion may result. This is transferred to a bottle, the spirit of lavender is next added, then the ferrous sulphate dissolved in 50 Cc. of rose water, and finally sufficient rose water to bring the volume up to 1000 Cc. The reaction between the potassium and iron salts results in the formation of ferrous carbonate and potassium sulphate; the former separates as a greenish precipitate gradually darkening in color, while the latter remains in solution. The sugar is added to prevent oxidation of the iron compound, which it does to some extent; but unless the mixture be kept in filled and well-corked bottles it soon changes, and hence it should be freshly made when wanted. The spirit of lavender ordered is the official alcoholic solution of lavender oil, and must not be confounded with compound tincture of lavender, known to many simply as spirit of lavender; the latter would form an inky mixture with the iron compound present.

Compound Mixture of Glycyrrhiza, or Compound Licorice Mixture.—This well-known preparation, popularly called Brown Mixture, is made by dissolving the pure extract of licorice and acacia in 500 Cc. of water and then adding the other ingredients in the order named in the formula, the required volume of finished product being obtained by the addition of sufficient water. The resulting mixture is rather an unsightly preparation, and not in keeping with modern elegant pharmacy; it may be improved in appearance by setting it aside for a couple of days with frequent agitation, then adding some paper pulp and filtering. The formula suggested by Charles Tilyard, in 1860, yields an equally efficient and far handsomer preparation; it prescribes a larger proportion of sugar (by no means a disadvantage), and can be improved still further by the use of purified extract of licorice, as now ordered by the Pharmacopœia. The formula, as modified and adapted to the proportions of the Pharmacopœia, is as follows: Dissolve 30 Gm. of pure extract of licorice in 300 Cc. of water: add 120 Cc. of camphorated tincture of opium, 60 Cc. of antimonial wine, and 30 Cc. of spirit of nitrous ether, and set the mixture aside for twelve or twenty-four hours, with occasional agitation; filter the liquid into a bottle containing 30 Gm. of granulated acacia and 600 Gm. of granulated sugar, and wash the filter with sufficient water to bring the volume of the finished product up to 1000 Cc. The sugar and acacia are readily dissolved by agitation, the result being a thin, rich-looking, clear syrup which keeps admirably.

Mixture of Rhubarb and Soda.—Ordinarily, when fluidextract of rhubarb is mixed with water, copious precipitation of resinous and extractive matter at once ensues; but this is prevented in the official mixture by the alkali bicarbonate, and the solution is preserved by the glycerin subsequently added. It keeps quite well, but is not often prescribed.

CHAPTER XXVIII.

PILLS.

PILLS are a very convenient mode of administering medicines, the chief advantages lying in the small bulk to which the medicine is reduced and the almost complete disguise of bitter and nauseous remedies, by reason of their being swallowed without previous mastication. Pills are admirably adapted for the administration of heavy metallic substances not readily suspended in liquids, and also in cases in which the action of the medicine is to be slow, or even retarded until it reaches the lower bowel. The usual shape given to pills is that of a sphere or globe, although an ovoid shape is also sometimes used, and, in a few cases, even the lenticular shape is preferred. Their weight ranges from less than 0.06 Gm. to 0.3 Gm. (1 gr. to 5 gr.) for vegetable substances, or about 0.5 or 0.6 Gm. (8 to 10 grains) for heavy mineral compounds; if a pill exceeds this weight, it is called a *bolus*. Boluses are occasionally made weighing 1.3 or 2.0 Gm. (20 or 30 grains) each, and are often of a softer consistence than pills. Very small pills coated with sugar are called *granules*.

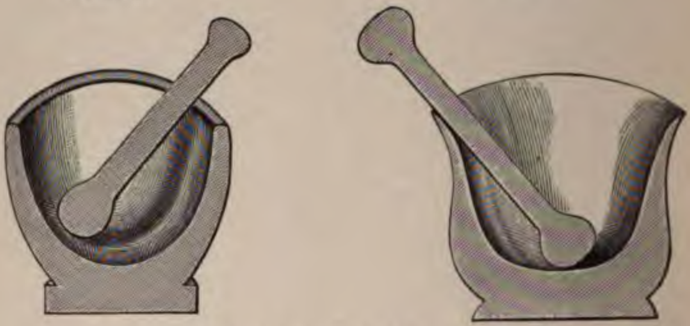
Although of late years the extemporaneous preparation of pills has materially decreased, and in some localities is almost unknown, the operation must yet be considered one of the most important pharmaceutical manipulations, and is deserving of a lengthy discussion, because the opportunities for a practical acquaintance with the details of the work are growing less day by day, owing to the untiring efforts of manufacturers to induce physicians to specify factory-made pills in their prescriptions.

The most important step in the preparation of pills is the formation of a proper mass, which should consist of a paste sufficiently plastic to admit of being moulded without adhering to the mould, yet firm enough to prevent the pills from losing their original shape. Although a firm consistence should characterize every well-made pill-mass, its ready disintegration and solution in the fluids of the stomach and bowels are of paramount importance, and it is essential so to unite the ingredients of a pill-mass that ready separation in the stomach may be assured. Plasticity is that peculiar condition in which adhesiveness and firmness are properly balanced; the former of these properties is due to a partial softness, which enables the particles of the mass to adhere to one another, thus imparting tenacity to the whole. Some substances possess this adhesiveness in themselves, but require the addition of a liquid—water or alcohol—in order to develop it; as, for instance, gums and resinous drugs. Other substances possess no inherent adhesive properties, and in such cases it becomes necessary to impart tenacity to them by the addition of some adhesive liquid or solid material; such substances are camphor, calomel, bismuth salts, some saline or vegetable powders, reduced iron, and the like. Firmness in a pill-mass is as essential as adhesiveness, and while the latter is brought about by a state of partial solution or fluidity, yet, inversely, the insolubility of some particles is necessary for the required firmness. The substances added to pill-masses as adhesive or absorbent agents are known as excipients, and must be employed judiciously, so that the constituents of the mass be not modified in their action nor the bulk unnecessarily increased. After each addition the mass should be well kneaded, which, itself having a softening influence by reason of the heat generated, enables the operator to judge of the condition of the mixture. Whenever possible, all constituents of a pill-mass should be reduced to very fine powder before the addition of any excipient, as only in this condition can the homogeneity of the mass, as well as the subsequent accurate division of doses, be assured. Small quantities of potent remedies, such as alkaloids, narcotic extracts, toxic chemicals, etc., are preferably triturated with a little sugar of milk before mixing them with the other ingredients, to facilitate uniform distribution.

Whenever substances are ordered in a pill-mass in quantities which it is impossible or inconvenient to weigh accurately, as, for instance, aconitine 0.004 Gm., digitalin 0.012 Gm., atropine sulphate 0.020 Gm., veratrine $\frac{1}{24}$ grain, strychnine $\frac{1}{12}$ grain, morphine sulphate $\frac{1}{6}$ grain, etc., a dilution of the substance should be made with sugar of milk in such proportions that a conveniently weighable quantity shall contain the desired amount of the active ingredient. Thus, if 0.004 Gm. of any substance is wanted, carefully triturate 0.050 Gm. of the substance with 0.450 Gm. of sugar of milk (or 0.100 with 0.900 Gm. if more convenient); each 0.010 Gm. of the mixture will then contain $\frac{1}{50}$ of 0.050, or 0.001 Gm. of the medicinal agent, and hence 0.040 Gm. will contain 0.004 Gm., or 0.120 Gm. will contain 0.012 Gm., or 0.200 Gm. will contain 0.020 Gm., etc. If $\frac{1}{24}$ of a grain of any substance is needed, triturate $\frac{1}{2}$ grain of it with $11\frac{1}{2}$ grains of sugar of milk (or 1 grain with 23 grains if more convenient), and each grain of the mixture will contain $\frac{1}{24}$ grain of the active ingredient, or $1\frac{1}{2}$ grains will contain $\frac{1}{16}$ grain, or 2 grains will contain $\frac{1}{12}$ grain, or 3 grains will contain $\frac{1}{8}$ grain, or 4 grains will contain $\frac{1}{6}$ grain, or 6 grains will contain $\frac{1}{4}$ grain, etc. In a similar manner other dilutions may be made to obtain a different number of milligrammes or different fractions of a grain.

Pill-masses should always be made, according to the nature of the mass, either in iron or Wedgewood mortars, of the shape shown in Figs. 219 and 220, and the mixture should be frequently scraped from the pestle and the sides of the mortar with a stiff spatula so as to bring all particles repeatedly under the pestle. Trituration by means of a pestle is essential to produce a uniform mixture of the ingredients; and, moreover, it will be found that a mass can be formed in less time, with less excipient and less labor, in a mortar than on a pill-tile. Very simple combinations, such as blue mass and extract of colocynth, etc., may be effected on the pill-tile; but for all substances requiring uniform blending of fine powders, and similar cases, the use of the tile is to be condemned. Unfortunately, the misuse of the pill-tile is a characteristic of many American pharmacists. One rule should be strictly observed in making every pill-mass, namely: *Never use the spatula with which the mass is scraped down for taking excipient from its container.*

Fig. 219. Fig. 220.

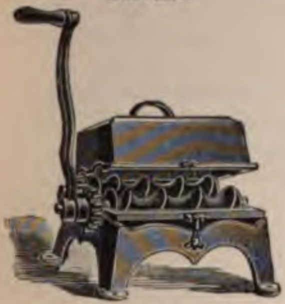


Sectional view of properly shaped pill mortars.

Large quantities of pill-masses which cannot be conveniently handled in a mortar are best made in a special apparatus known as a pill-mixer, operated by either hand or steam-power. As a rule, these kneading machines consist of smooth iron rollers (for white pill-masses hard-wood rollers are generally used), which revolve in opposite directions, some being so constructed that they can be heated, if necessary, by passing steam through them. The ingredients for the mass are first roughly mixed in a basin or tank and then repeatedly passed between the rollers until a uniform mixture has been produced. In Figs. 221 and 222 are shown two sizes of iron mixers for pill-masses, made by J. H. Day & Co., of Cincinnati, the smaller one having a capacity of 3 pounds and the larger of 30 pounds. The tanks are porcelain lined, and the corrugated rollers or mixers are galvanized. As shown in the illustrations, the machines are easily opened and taken apart for cleaning purposes. While mixing a mass the rollers turn toward each other, and while emptying, from each other. The finished mass can be easily removed by tilting the machine and at the same time causing the rollers to revolve slowly in a reverse direction.

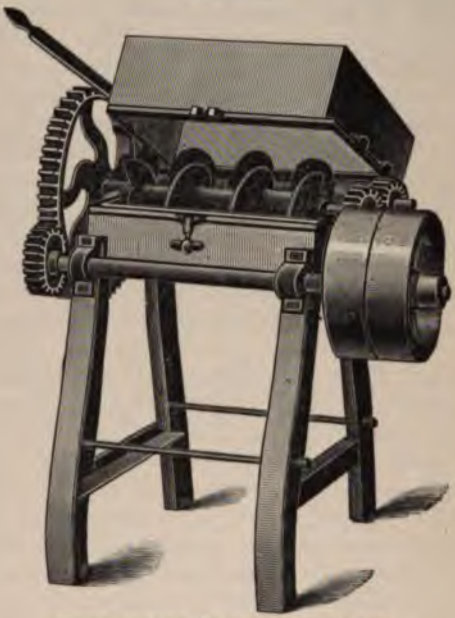
Excipients.—It being impossible to select one single substance as an excipient suitable for all pill-masses, owing to the variable properties of drugs and the many different combinations ordered by physicians, it is essential that the pharmacist be familiar with the peculiarities of each excipient, in order to use the same intelligently and advantageously. Excipients for pill-masses may be divided into three distinct classes, as follows:

FIG. 221.



Hand machine for mixing pill-masses.

FIG. 222.



Power machine for mixing pill-masses.

1. Those which are intended to develop adhesiveness, and hence act as solvents. To this class belong water, alcohol, diluted alcohol, glycerin, and a mixture of glycerin and water.

2. Those which are intended to impart adhesiveness; these may be fluid, semifluid, or solid. To this class belong syrup, glucose, honey, mucilage and syrup of acacia, mucilage of tragacanth, glycerite of starch, acacia with glucose or honey, tragacanth with glycerin, soap with water or diluted alcohol, extract of malt, confection of rose, manna and powdered elm-bark mixed with tragacanth; the last named requires the addition of syrup or glycerin and water.

3. Those which are intended to act simply as absorbents of excessive moisture and, in a few cases, impart adhesiveness to the mass at the same time. To this class belong powdered liquorice root, soap and liquorice root, calcium phosphate, powdered orris root, powdered tragacanth, powdered elm-bark, starch, and powdered marshmallow.

The first class, solvents, are employed in many cases in which physicians order vegetable powders in connection with soap or solid extracts, the latter in insufficient quantity to form a good mass. Solvents must be added to pill-masses with great care, especially when water or glycerin is used with soap or extracts; by adding the fluid in drops and working the mass well after each addition, the required consistence will soon be developed, and a firm yet plastic mass be obtained, while an excess of moisture causes a softening of the mass, which frequently increases, and prevents the formation of perfect pills, besides requiring the addition of absorbent powders, which add to the bulk of the mass.

The second class, adhesive excipients, are more extensively used than any other, because the majority of substances prescribed in pill form do not possess inherent adhesive properties, or at least insufficiently, for properly massing the ingredients. Mucilage and syrup of acacia are the least desirable of the class, unless the pills are for immediate use, as pills made with acacia are prone in time to become very hard; the addition of glycerin, however, obviates the difficulty. Syrup or glucose is usually preferred to water for massing vegetable powders, in the absence of soap or solid extracts. Tragacanth with glycerin can be most conveniently used in the form of a jelly, made by triturating 85 grains of powdered tragacanth with 6 fluidrachms of glycerin and 1 fluidrachm of water; it is an excellent excipient for the salts of quinine, salol, acetanilid, sodium salicylate, iodoform, calcium sulphide, and also gallic and tannic acids; but for cinchonidine sulphate or salicylate, acacia with glucose or honey is preferable. Soap with water or diluted alcohol is the best excipent for aloes, rhubarb, and the various gum-resins; it cannot, however, be used with soluble metallic salts, as those of iron, lead, copper, etc., owing to the formation, by mutual decomposition, of metallic oleates, which cause the mass to crumble.

The necessary precaution regarding the use of water in conjunction with soap has been mentioned above; an excess of the former invariably causes trouble. Manna is very desirable for massing reduced iron or manganese dioxide when these are prescribed alone. Extract of malt is very similar to glucose in its applicability, but can be used only for dark-colored masses. Confection of rose, at one time much esteemed as an excipient for mixtures of vegetable powders and metallic salts, has now almost gone out of use. For the valerianates of iron, quinine, or zinc, no better excipient can be used than acacia and alcohol in the following proportions: Iron, quinine, or zinc valerianate, 30 grs.; powdered acacia, 10 grs.; alcohol, 5 minims. Camphor and monobromated camphor can be made into very satisfactory pill-masses by the addition of soap and oil of sweet almond or castor oil; about 1 grain of soap and 2 drops of oil will be sufficient for 12 grains of camphor.

As an excellent adhesive agent for heavy metallic salts, such as bismuth subnitrate or calomel, as well as for the scale salts of iron and troublesome combinations like capsicum, camphor, and lead acetate, Mattison's excipient powder will be found very serviceable; it consists of 1 part of powdered tragacanth and 7 parts of finely powdered (No. 80) elm-bark. Only a very small proportion of the powder is required, thus: 3 grains for 60 grains of bismuth subnitrate, calomel, cerium oxalate, iron by hydrogen, or equal parts of camphor and lead acetate; 6 grains of the powder for 60 grains of dried ferrous sulphate, the scale salts of iron, or equal parts of camphor and capsicum, etc. In all cases in which this excipient powder is employed, the mass should be made up rather soft with syrup, otherwise it is likely to crack or crumble while the pills are being formed; pills thus made become sufficiently firm and retain their original shape, on account of the fibrous and adhesive character of the excipient. Hager has recommended a similar powder, composed of 1 part of powdered marshmallow root, 1½ parts of powdered tragacanth, and 6 parts of powdered orris root; this powder can be used like the preceding, and is better adapted to white pill-masses. In place of syrup, a mixture of 2 volumes of glycerin and 1 of distilled water may be used for pills which it is desired to keep soft.

At one time, crumb of bread was ordered quite frequently as an excipient for pill-masses, particularly in cases in which it was intended at the same time to serve as a vehicle for the administration of potent remedies, as in the case of mercuric chloride, strychnine, etc. In place of bread-crumb, which is not always available, either of the excipient powders mentioned above may be used, or a mixture of 1 part of tragacanth and 3 parts of starch, the mass to be made with glycerin and water, as before stated. The salts of quinine and cinchonidine are frequently prescribed in pill form, in combination with aromatic or diluted sulphuric acid, the quantity of acid being often left to the judgment of the dispenser. As a rule, from one-third to one-half as much acid as alkaloidal salt is sufficient to make a satisfactory mass, depending somewhat upon the condition of the atmosphere. The mass must be rolled out as soon as it becomes plastic, while still a little soft, otherwise it becomes dry and crumbly; in the latter case, the addition of a drop or two of syrup, or a very small quantity of glycerite of starch, restores the proper condition. Quinine sulphate triturated with one-sixteenth of its weight of tartaric acid becomes damp and adhesive, and upon the further addition of a small quantity of glycerin (about 15 or 16 drops to 100 grains of quinine sulphate) yields an excellent mass, the pills being small and firm. If kept in a cool, dry place, such pills retain their original condition for a long time; but if carelessly preserved, they absorb moisture and become soft, and are apt to stick together. Although strong mineral acids are rarely prescribed in pills, they are occasionally used, in combination with pepsin and vegetable powders, in prescriptions written in Germany; the excipient powder mentioned in the preceding paragraph, together with glycerin and water, will yield a good mass.

Easily reducible substances, like silver nitrate, potassium permanganate, silver oxide, gold chloride, etc., cannot be massed with the usual excipients, as they need some adhesive agent which will not cause decomposition. The most available substances are white clay (kaolin) and water, which form a plastic mass, but one requiring quick manipulation, as it soon becomes dry and crumbly. The following excipient, proposed by M. Carles for pill-masses of this character, namely, a mixture of 2 parts of kaolin and 1 part each of anhydrous sodium sulphate and water, has proved satisfactory. Sixty grains of kaolin and 30 grains of the sodium sulphate require 40 minims of water to form a plastic mass, which dries slowly and retains its plasticity for six or eight minutes; it admits of much better manipulation than do clay and water alone, and the pills, when formed, soon become hard and retain their shape, owing to the assumption of the crystallized state by the anhydrous sodium sulphate under the influence of water. When potassium permanganate is to be made into pills with this excipient, a larger quantity of water must be used; the best plan is to rub 30 grains of potassium permanganate into fine powder, mix well with 30 grains of kaolin and 15 grains of anhydrous sodium sulphate, and then mass with sufficient water, usually 25 to 30 minims. A mixture of equal parts of kaolin, or fuller's earth, soft petrolatum, and paraffin, forms a most excellent excipient for this class of pills; or the medicinal agent, in fine powder, may be incorporated with its own weight of lanolin, or wool fat, deprived of its water, and then sufficient kaolin be added to form a mass. Lanolin is indifferent toward silver nitrate and potassium permanganate (Hager). Another satisfactory method is to mix potassium permanganate with one-half or the whole of its weight of kaolin, and then mass with one-fourth its weight of soft petrolatum.

When deliquescent substances, or such as slowly volatilize upon exposure to air, are ordered in pill form, a mixture of potassium borotartrate with half its weight of water will prove a good excipient; about $\frac{1}{8}$ of a grain of powdered tragacanth should be added for each pill, and the mass must be quickly formed and rolled out; 60 grains of hydrated chloral or 30 grains of potassium iodide require 2 drops of the excipient. Even potassium acetate has been made into satisfactory pills by the aid of potassium borotartrate, 18 parts of the former and 3 parts of the latter being used with 1 part of water. All such pills should be dispensed in bottles.

The third class, absorbent excipients, are frequently required to supply the necessary firmness to a pill-mass, so that the original shape given to the pills may be retained. The addition of absorbent powders must be made judiciously, so as to avoid an unnecessary increase in the bulk of the mass, and the quantity used should be noted on the prescription, so that in case of a repetition pills of the same size may be dispensed. The reckless use of solvent as well as absorbent excipients is one of the chief errors of inexperience, and ofter causes much trouble. Some absorbent powders, such as starch, calcium phosphate, magnesium carbonate, licorice root, and orris root, possess little or no adhesive properties, and if used in excess will cause the mass to crumble; others, like marshmallow root, acacia, and elm-bark, containing much mucilaginous matter, if used in excess, form hard and slowly soluble combinations.

For pill-masses containing an excessive quantity of soft, solid extracts, powdered licorice root will be found very desirable and preferable to powdered elm-bark, unless metallic salts are present in large proportion. For volatile oils, creosote, and liquid oleoresins, soap is decidedly the best excipient, as it emulsionizes these and prevents their separation during subsequent manipulations; from ½ to 1 grain of soap is necessary for each minim of oil, and stearin or curd soap will be found preferable to olive-oil soap. In the absence of any vegetable powder in the prescribed combination, the addition of powdered licorice root is desirable, and a mixture of 1 part of soap and 5 parts of licorice root forms a convenient excipient, of which 3 grains should be used for each minim of volatile oil; if necessary, water or diluted alcohol may be used to facilitate massing. The incompatibility of soap and soluble metallic salts in pill-masses has been noted in a previous paragraph. For creosote, when ordered by itself, powdered licorice root and water are very serviceable; 2 grains of the powder with a little water are sufficient for each drop of creosote. Carbolic acid can be treated like creosote, and soap will be found to bind it very nicely.

Tar, when prescribed in pill form, either alone or in connection with other remedial agents, requires the addition of an absorbent; magnesium carbonate and powdered licorice root have been recommended, but calcium phosphate, used in twice the weight of the tar, has been found more satisfactory, yielding a firm yet plastic mass. Pills thus made retain their original shape and disintegrate readily in water. For making pills of mercurial ointment the same excipient has been used with success.

Hager has suggested a mixture of equal weights of yellow wax and starch, in the form of powder, as a superior adhesive and absorbent excipient for numerous troublesome pill-masses; starched wax is decidedly preferable, as an excipient, to wax with an addition of some fibrous vegetable powder, as pills made with the former disintegrate more rapidly, and the wax, being in a state of fine division, is less liable to cause intestinal trouble. From 3 to 5 grains of starched wax will yield a satisfactory mass with 1 grain of each of the following substances (Hager): carbolic acid, apiol, oleoresin of male fern, guaiacol, creosote, croton oil, terpinol, and oil of tar. Starched wax may be prepared by thoroughly drying yellow wax, in the form of thin shavings, under a paper cover in a dark place, and then rubbing into powder with an equal weight of rice-flour.

Unless some other substance is present, as an oleoresin or a volatile oil, whereby the melting-point of the mixture is brought down to about 38° C. (100.4° F.), wax is very undesirable in pill-masses on account of its difficult disintegration, which may cause pills made therewith to pass through the body unaltered. When wax is directed to be used in a pill-mass, it should be melted at a moderate heat and then mixed with any oil or oleoresin ordered, before the solid ingredients are added.

Powdered tragacanth may sometimes be employed as an absorbent when it is desired to impart adhesiveness to a very moist mass without materially increasing the bulk. The mixture of tragacanth and powdered elm-bark, previously mentioned, is, however, generally to be preferred. The compound tragacanth powder of the British Pharmacopœia, composed of 1 part each of powdered tragacanth, powdered acacia, and starch, and 3 parts of powdered sugar, forms an excellent absorbent and adhesive agent, and pills made with this excipient disintegrate readily.

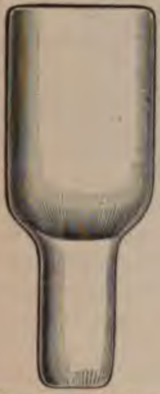
A mixture of equal parts of finely powdered elm-bark and starch will be found a most desirable excipient for soft pill-masses containing iodine or iodide of iron; the mass should be rolled out while still moderately soft, as the pills will harden subsequently. Pill-masses containing free iodine should invariably be made with the addition of starch, which, combining with the iodine, prevents its irritating effect on the mouth and throat; the union between the starch and iodine is very feeble, and the latter will be liberated by the warm liquids of the stomach.

In a few cases the addition of any excipient is superfluous, as when lupulin and camphor are ordered together in pill-form. The simple trituration of powdered camphor with lupulin causes the resinous matter to soften, and an adhesive mass is quickly obtained which hardens on standing. All solvents, like ether, alcohol, and diluted alcohol, must be avoided, but a very small quantity of elm-bark may sometimes be added with advantage in very warm weather.

Mortars and other utensils used in making pill-masses are sometimes cleaned with great difficulty, on account of the stain imparted by certain chemicals. As a rule, plain water, cold or hot, will suffice to remove the slight remnants of a pill-mass, especially if allowed to stand in the mortar for a short while; but in some cases the addition of lye (caustic potassa or soda solution) becomes necessary to soften hard resinous deposits. The persistent odor of volatile oils is best removed with a little alcohol after the mortar has been well washed with water. A few drops of oil of turpentine promptly remove the odor of iodoform. Metallic stains, as a rule, are dissolved quickly by a little strong hydrochloric or nitric acid. Manganese dioxide stains disappear at once if treated with coarsely powdered ferrous sulphate, sulphuric acid, and water; while potassium permanganate stains yield readily to a solution of oxalic acid.

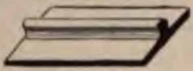
Division of the Pill-mass.—After the mass has been properly prepared, it is transferred to a pill-machine or a graduated glass or porcelain tile, to be rolled out, by means of a flat piece of hard wood, into a rod or pipe of uniform thickness, which is then divided into the requisite number of pieces. Steel spatulas are used by many for rolling out the mass, but are not so desirable as a wooden roller, since the width of the spatula permits of covering only a small part of the mass at a time, hence irregularity in the thickness of the cylinder frequently occurs. A little pressure must be applied when rolling out the mass, both on the pill-machine and tile. Figs. 223 and 224 represent wooden pill-mass rollers, the long one with the handle having the more convenient shape.

FIG. 223.



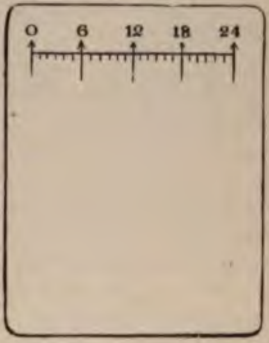
Wooden pill-roller.

FIG. 224.



Pill-roller.

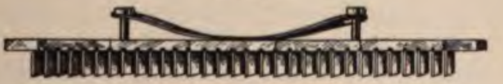
FIG. 225.



Pill-tile, graduated.

A small number of pills may be conveniently divided on a pill-tile (Fig. 225), but for a larger number a pill-machine will be found preferable, particularly if the weight of the pills corresponds to the size of the grooves, for then the perfect rounding of the pills can be readily effected by continued rolling in these grooves. In order to insure greater uniformity in cutting the mass on a pill tile into the required number of parts, use may be made of either of the two devices shown in Figs. 226 and 227. The Livingston pill-cutter

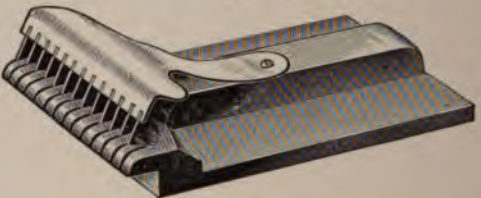
FIG. 226.



Livingston pill-cutter.

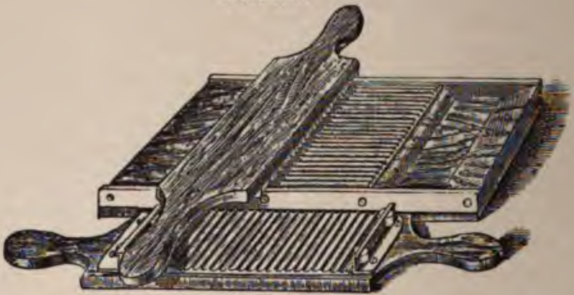
may be used to cut 24 parts at one time by simply pressing the steel cutters into the pill-mass after the same has been rolled out to the required length by means of a wooden pill-paddle; the separate pieces may then be quickly ejected by means of a slotted metallic strip operated by a spring on the top of the bar. The Diamond pill-cutter is combined with a flat wooden roller for rolling the mass out to the required length, which is then brought under the projecting cross-piece and the metal cutters pressed down upon it; as the metal plate, to which the cutters are attached, rebounds to its original position, the latter are stripped of any adhering pieces of mass by the projecting cross-piece, through the slots of which the cutters pass. Fig. 228 represents a complete pill-machine. It consists of a smooth, hardwood rolling-board encased in metal and provided with a grooved metal plate; to the roller, which is likewise made of hard wood, is attached a similar metal plate, the grooves of which correspond exactly to the grooves of the plate on the board, being adjusted to the size of pills of certain weights, as 1, 2, 3, or 5 grains. To facilitate the motion of the roller, it is frequently provided with two little metal wheels on each side of the grooved plate, as may be seen in the illustration. When the roller is in use, these bear against the metal casing of the rolling-board and thus enable the roller to travel uniformly.

FIG. 227.



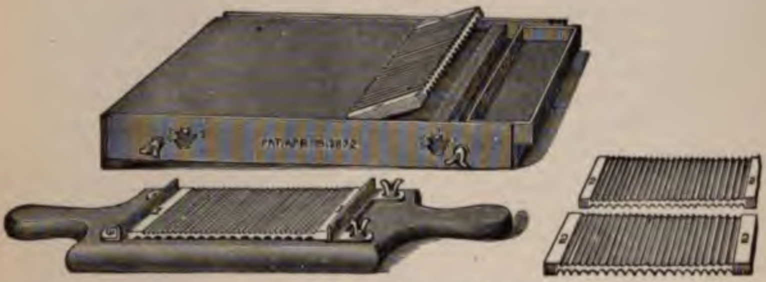
Diamond pill-cutter.

FIG. 228.



The best pill-machine is the "Cooper patent" (Fig. 229), the woodwork being of mahogany and the metallic parts of brass. This machine has two sets of reversible grooved plates, on which four different sizes of pills can be made—1, 2, 3, and 5 grains; the plates being quickly removable and adjustable. The sides of the rolling-board are so constructed that they can be raised or lowered by means of winged screws, which allows the mass to be rolled just the thickness required for each respective size of pill, thereby insuring always the full number of perfectly round pills.

FIG. 229.

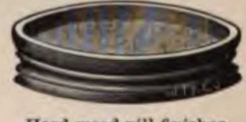


Cooper's patent pill-machine.

After the mass has been properly rolled out to the length of the desired number of pills, it is laid upon the grooved plate of the board, and divided by placing the other cutter over it and drawing the same forward and backward with slight pressure.

When the pill-mass has been divided on a pill-tile, and also when the pills are larger or smaller than the grooves of the machine, it becomes necessary to impart a spherical shape to the pieces, by appropriate rolling between the thumb and first and second fingers, after which the pills should be placed under a pill-finisher and completely rounded by rotary motion of the same with some pressure. It is better to move the finisher about in curvilinear figures like the figure 8, instead of giving it a constant circular motion, so that the pressure may be uniform at all points. Pill-finishers usually consist of a circular piece of hard wood, with a smooth rolling surface and a projecting margin for the purpose of confining the pills; several sizes are required to suit different sizes of pills. Fig. 230 represents a convenient pill-finisher suitable for two different sizes, as the upper and lower margins project to different lengths.

FIG. 230.

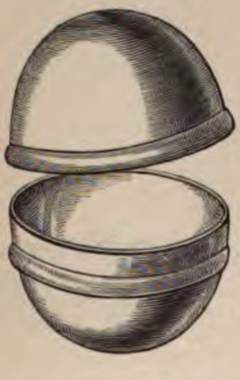


Hard-wood pill-finisher.

Pill-dusting.—The pill-mass, being plastic and adhesive, is prone to adhere to the slab and the fingers while being rolled out and shaped into pills. This may be prevented by the use of a fine powder, which should be wholly inert, unless otherwise directed by the physician. Among the most suitable powders are lycopodium, licorice root, and starch. The former is particularly desirable on account of its fineness and uniformity, its slight adhesiveness, and its tastelessness. Powdered starch should be used with all white pill-masses, Bermuda arrow-root being the best for the purpose. Only in exceptional cases is the addition of dusting-powder to the pills in the box justifiable; the pills should receive a sufficient coating of the powder under the finisher; then, if the mass has been properly made, there will be no likelihood of the pills adhering, hence no occasion for putting an excess of powder in the box. Magnesia and magnesium carbonate are not well suited for dusting-powders, and should, moreover, be used with due care, on account of the possible chemical effect upon the ingredients of the pills. Powdered talc (soapstone) is likewise serviceable, having the advantage of imparting a very thin, opaque, and tasteless coating to the pills, without impairing their solubility in the stomach; it is particularly suited for pills of silver nitrate and the like. When asafetida or other nauseous substances are given in the form of pill, the odor may be either entirely disguised or considerably modified by the use of powdered cinnamon, aromatic powder, ginger, or similar material.

Pill-coating.—The plan of coating pills with various substances, with a view to mask the odor and taste of nauseous medicines, is by no means a novelty, having been practised more than fifty years ago. At one time the silvering or gilding of pills was of frequent occurrence, but at present it is but rarely employed. Pills to be thus coated must be made firm and rolled perfectly smooth, if possible without any dusting-powder; they should be very slightly dampened with a mixture of equal parts of alcohol, syrup, and mucilage of acacia and then placed in a suitable apparatus consisting of two hollow hemispheres of hard wood or horn, as shown in Fig. 231. Silver or gold foil is added, when, the apparatus having been closed, a rapid rotary motion will in a very short time cause the pills to take on a uniform coating of the metal; should some of the pills receive only a partial covering, more foil must be added and the rotary motion repeated. As a rule, one leaf of silver or gold will cover a half-dozen 3-grain pills. Glycerin should not be used as an excipient for pills which are to be silver- or gold-coated, as it will lessen the brightness of the metal.

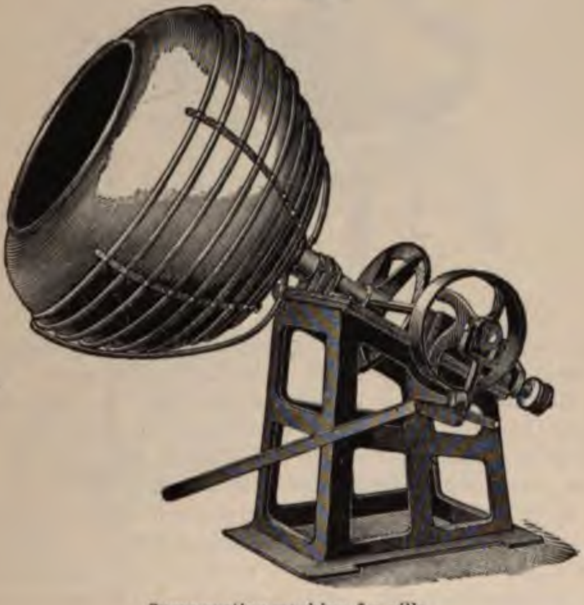
Fig. 231.



Sugar-coating is a process which is not readily applicable to the operations of the pharmacist, requiring experience and practice to insure success. It partakes of the confectioner's art, although the coating of pills with sugar requires somewhat more care, on account of the absence of starch or flour, which generally make up a part of the confectioner's coating. Sugar-coating of pills on a large scale is done in hemispherical copper pans made to revolve slowly within a coil of steam-pipe supplying the necessary heat for evaporation of the moisture; the pills, which should be well air-dried, are placed in the pan, and a quantity of simple syrup or of a mixture of syrup and mucilage of acacia is poured on, the pan being kept in constant rotary motion until the pills are dry. The addition of syrup is repeated until a sufficiently thick coating has been deposited on the pills, and this can be determined only by experience.

Sugar-coating can be more successfully performed with a large quantity of pills than with a small number, as the deposit of sugar takes place more uniformly, and the mutual attrition of many pills insures a smooth surface. Fig. 232 represents a sugar-coating pan in use in large manufacturing establishments; as seen in the illustration, it is operated entirely by steam-power. For small operations it will be found desirable to dampen the pills with diluted mucilage of acacia or egg-albumen and then rotate them in a tinned-copper or porcelain dish containing either finely bolted sugar or a mixture of acacia 1 part and sugar 5 parts, or of sugar 2 parts, sugar of milk 1 part, and purified talcum 1 part. With care and practice very fair results may be obtained, although the pills should not be expected to look so perfect as those coated by machinery. A small apparatus has been devised in England for facilitating the

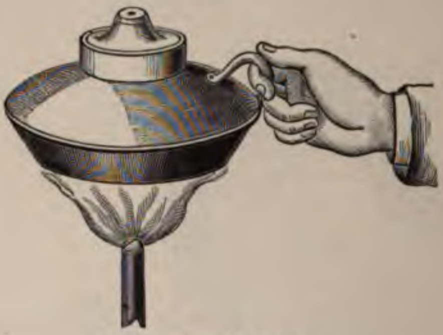
FIG. 232.



Sugar-coating machine for pills.

sugar-coating of pills at the dispensing-counter; it is shown in Fig. 233, and consists of a flat-bottomed, tinned-copper pan, with a hinged cover. The pills having been dampened as directed, may be placed in the pan with the sugar and rotated while a gentle heat is applied, which facilitates the drying of the coating; when dry, the process can be repeated until a perfect, hard, white coating is obtained. Sugar-coated pills do not at first have the familiar glossy appearance, but are dull when taken from the coater; they are then shaken with pieces of paraffin, which causes a minute film of the latter to be deposited on the sugar, and thus the desired gloss is produced.

FIG. 233.

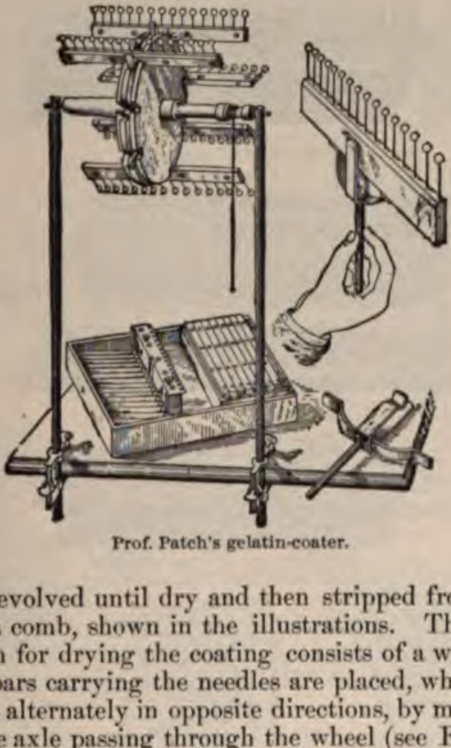


Small sugar-coating pan.

Gelatin-coating is more readily applied than sugar-coating, but, like the latter, requires practice to insure proficiency. The chief difficulty lies in the drying of the coating after the pills have been dipped into the solution of gelatin; the pills must be kept in motion while the gelatin cools, otherwise the coating will not be uniform. Pills to be gelatin-coated must be firm, dry, and free from dusting-powder; if glycerin is used as an excipient, it is likely to soften the gelatin-coating, causing the pills to stick together. For pills containing strongly odorous substances, such as asafetida, sumbul, iodoform, the valerianates, etc., gelatin-coating is decidedly inferior to sugar-coating, as the odor penetrates gelatin far more rapidly than sugar. The manner of coating the pills on a large scale is identical with that used for only a dozen pills, namely, the pills are impaled upon long, thin needles, to the depth of about $\frac{1}{16}$ of an inch, and then immersed in a solution of gelatin kept fluid by means of a water-bath; in order to avoid contraction and cracking of the gelatin upon cooling, mucilage of acacia is usually added to the solution, and, by some, syrup also. The rapid drying on a large scale is effected by placing the pills soon after they have been dipped, while still on the needles, in specially constructed drying cases connected with an exhaust fan, by means of which air is rapidly drawn through the cases, and the moisture is thus removed.

For small operations various devices have been suggested for drying the gelatin-coating, no one of which can be said to be the best, as pharmacists prefer that apparatus with which they have become most familiar by practice. The gelatin solution should be kept at a temperature of between 72° and 82° C. (161.6° and 179.6° F.), so that it may not be too thick when the pills are immersed, and any scum or froth forming should be carefully pushed aside before the pills are dipped. Figs. 234, 235, 236, and 237 represent the four leading styles of gelatin-coating apparatus in use among pharmacists in this country. In three of them the pills are taken up on the needles from a tray provided with grooves, in which the pills have been placed, and, after they have been dipped into the gelatin solution, are revolved until dry and then stripped from the needles by means of a comb, shown in the illustrations. The arrangement of Prof. Patch for drying the coating consists of a wheel with slots, in which the bars carrying the needles are placed, when the wheel is made to move alternately in opposite directions, by means of a string attached to the axle passing through the wheel (see Fig. 234). The gelatin solution recommended by Prof. Patch is made as follows: Macerate 2½ ounces (av.) of French gelatin (gold label) with 7 fluidounces of distilled water, and when soft, dissolve by aid of a hot water-bath; add 2 drachms of boric acid, and finally 2 fluidounces of mucilage of acacia; strain the mixture.

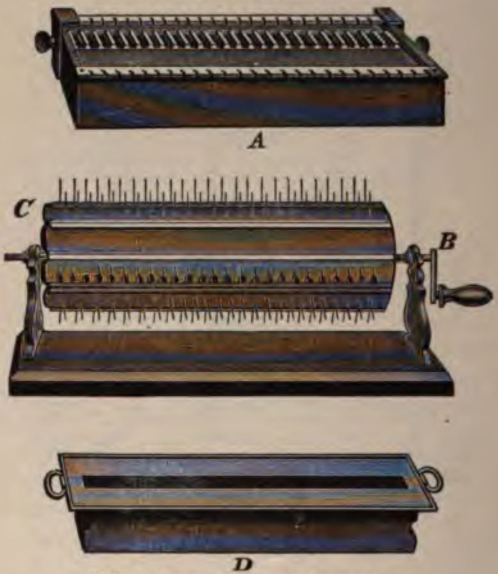
FIG. 234.



Prof. Patch's gelatin-coater.

The "Porcupine" gelatin-coater (Fig. 235), designed by C. C. Wells, consists of a wooden tray, *A*, provided with grooves and a gauge for regulating the depth to which the needles shall enter pills of different sizes, and also a brass comb for disengaging the pills from the needles; a drying cylinder, *B*, provided with T-shaped rails on its rounded cylinder, which form grooves for receiving the needle-bars *C;* a water-bath and solution-holder, *D*, the latter being a trough in the cover of the bath and kept at the proper temperature by the aid of heat. After the needle-bars carrying pills have been placed in the grooves of the cylinder the latter is kept revolving, by means of the crank on the side (larger machines are operated by clock-work attachments), at the rate of about 50 revolutions a minute, until the pills are dry enough not to stick together when taken off the needles. Wells recommends the following solution for gelatin-coating: Dissolve 2 drachms of acacia in 1 fluidounce of water, and add 1 ounce (av.) of Cox's gelatin, 2 fluidounces of water, and 1 fluidounce of simple syrup; dissolve by heat and strain.

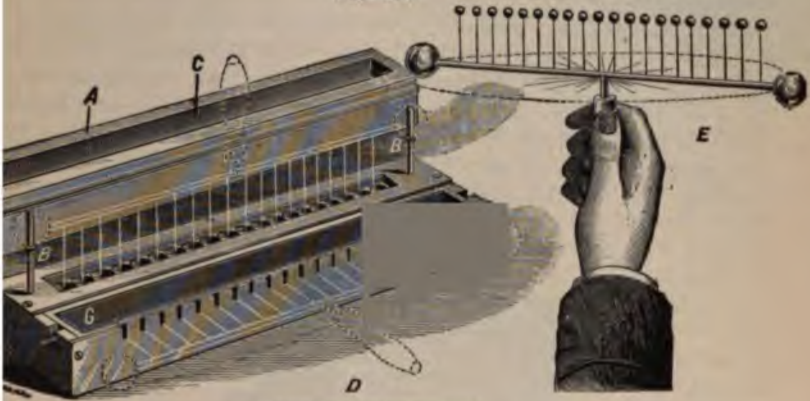
FIG. 235.



Wells' "Porcupine" gelatin-coater.

The gelatin-coater of W. C. Franciscus (Fig. 236) resembles the other two, except in the provision for drying the coating on the pills, which must be done by rapidly twirling the needle-bars centred on a pivot with the hand, until the pills are sufficiently dry to be removed. The different steps of the operation are shown in the illustration: *A* represents a water-bath, and *C* the solution-holder resting in the same; *BB* shows the position of the needle-bar in the act of impaling the pills which have been placed in the pressions in the tray, the balls on the ends of the bar insuring curacy in centring the pills with the needle-points, by slipping er the rods *B* and *B*. At *E* is shown the manner of revolving

Fig. 236.

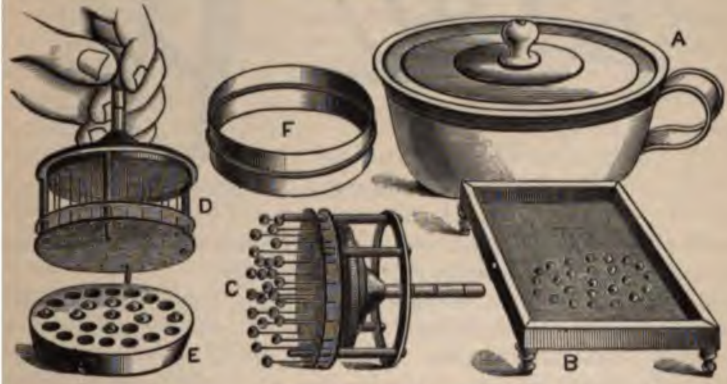


Franciscus' gelatin-coater.

pills, after they have been dipped, by means of the pivotal ndle *D*. When sufficiently dry, the pills are stripped from the edles by means of the comb attached to the tray *G*.

Maynard's gelatin-coater (Fig. 237) is not provided with a ooved tray from which the pills are taken up, but, instead, the

Fig. 237.



Maynard's gelatin-coater.

ls are placed in depressions in a metallic plate, E, provided also th two holes to receive the guide-pins attached to the circular edle-holder D, and surrounded with a metallic ring, F, to prevent pills rolling off. When the needle-holder is not in use, the

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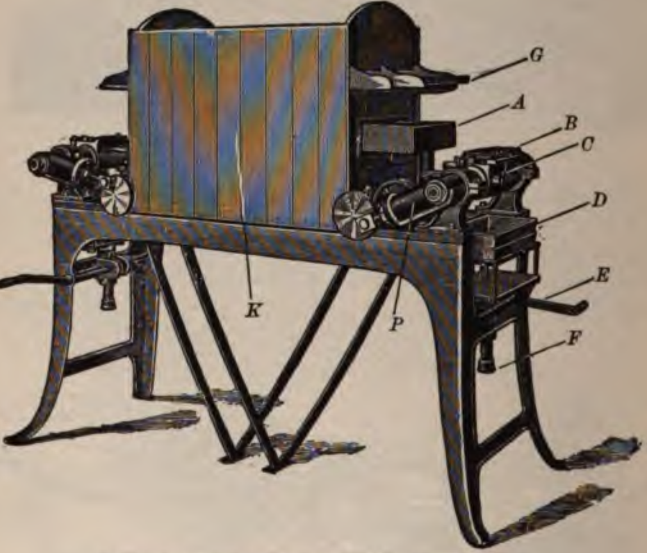
needle-points are drawn back behind the outer disk by means of the handle attached to the top, to which the needles are fastened. To impale the pills, the needles are depressed, passing through the perforations in the outer disk, and take up the pills as shown at C. The gelatin solution is contained in a covered agateware dish, resting in the copper water-bath A; after the pills have been dipped, the needle-holder is slowly revolved to facilitate the uniform distribution of the gelatin film. When the gelatin has set, the needle-holder may be laid aside, as shown at C, until the coating is sufficiently hard to allow the pills to be removed to the tray of wire gauze B, by grasping the circular plate on the needle-holder with one hand and pulling the handle upward with the other. It is always well to grease slightly with petroleum the perforated disk, through which the needles pass, to prevent the pills adhering.

FIG. 238.



Colton's machine for continuous gelatin-coating.

The application of a continuous coating of gelatin to pills without the use of needles is in successful operation at several large manufacturing establishments, but is not available at the dispensing-counter, since extensive steam-power machinery is necessary for the work. In Fig. 238 may be seen a cut of probably the only machine of its kind at the present time; it was designed by Arthur Colton, of Detroit, Michigan, and has a capacity of coating from 6000 to 10,000 pills per hour. This ingeniously constructed piece of machinery is operated by two female attendants in the following manner: The pills to be coated are placed in the drawer *A*, which is provided with a perforated plate in the bottom at the end projecting from the drying-kiln. The drawer *A* having been drawn out and so arranged that the perforated plate registers over a set of tubes on plate *B*, the pills are brushed through the perforations by means of a brush moving forward and backward in *A*, and are firmly held on the tubes by a vacuum, produced by means of the pump *P*. The tube-plate *B* is fastened by means of a clamp to the hood *C*, and by revolving the latter half-way, the plate is brought face downward over the pan *D*, containing the gelatin solution. By means of the handle *E* the pan *D* is then slowly raised far enough to immerse the pills half-way, which is regulated by the stop *F*, so as to avoid getting any gelatin solution on the tube-plate. The plate *B*, with the pills, is next raised and carefully placed in the slide *G*, and another tube-plate filled with pills as before, the operation of placing the pills on the tubes and coating them being continued until the supply is exhausted. As one plate after another is placed in *G* they are pushed forward through the kiln, where the coating is dried by currents of warm air sufficiently to allow the pills to be transferred to another plate at the other end, when the operation of dipping the other half of the pills is performed by the second attendant, and the plate now carrying the completely coated pills is returned through the kiln on a second slide running parallel to the first. When the pills again reach the first operator they are dry enough to be placed in trays.

In place of gelatin-coating at the dispensing-counter, the plan prevails in this country of disguising the disagreeable odor and taste of pills by enclosing them in gelatin capsules. These gelatin capsules are sold under the name of *empty capsules*, and consist of small cylinders closed at one end and provided with a shorter cylindrical cover; they occur in seven sizes, ranging from ⅝ inch to 1 inch in length, and are numbered respectively from No. 5 to No. 00; they are sold at fabulously low prices. The composition of the empty capsules made in this country is a mixture of gelatin and glycerin in variable proportions, dependent upon the character of the gelatin. The French Pharmacopœia recommends for hard capsules a mixture of 30 parts each of white gelatin, gum arabic, and sugar, 10 parts of clarified honey, and 100 parts of water, to be melted with the aid of a water-bath; for elastic capsules is recommended a mixture of 50 parts of white gelatin, 15 parts each of gum arabic and sugar, 12½ parts of glycerin, and 80 parts of water, to be likewise dissolved on a water-bath. Other authorities propose for hard capsules a mixture of 60 parts of gelatin, 10 parts each of acacia and sugar, and 50 parts of water; and for soft capsules a mixture of 50 parts of gelatin, 16 parts of sugar, 20 parts of glycerin, and 90 parts of water.

The capsules are made by dipping either metallic, bone, or wooden moulds, attached by means of handles to a suitable disk, into the melted gelatin mass kept at a temperature of about 40° C. (104° F.), and then rotating the moulds gently for a few minutes so as to insure a uniform film; if necessary, the immersion is repeated. To prevent adhesion of the gelatin solution to the moulds, the latter are rubbed with a soft oiled cloth before dipping them. After twenty or thirty minutes the gelatin film will have become sufficiently firm to allow the capsules to be stripped from the mould, and laid aside to dry in suitable closets provided with a draft of moderately warm air, any excess of gelatin being removed with an ivory knife before the capsule is taken from the mould.

As the object of capsuling pill-masses is to render the medicine as palatable as possible, care should be taken that the exterior of the capsule be not contaminated in any way with the material. This is best accomplished by dividing the mass into small cylindrical pieces, rounding off the ends of each, and then, after having washed the hands thoroughly, introducing the pieces, by the aid of a long needle, into the capsule held in the left hand, taking up the cover with two fingers of the right hand holding the needle and quickly slipping it into position, thus avoiding all contact of the mass with the exterior of the capsule. The habit of putting pills into capsules with the fingers is censurable and an evidence of bad training.

The filling of capsules with liquids is, as a rule, done in large manufactories, and for this purpose capsules of ovoid shape having a small orifice are selected; they are supported on trays or racks, and the liquid is introduced by means of a pipette or a syringe with a small nozzle. The orifice of the capsule is sealed with a little of the warm gelatin solution by means of a glass rod. When the pharmacist has occasion to dispense liquids in ordinary empty capsules, the best plan is to set the capsules up in a shallow box with a perforated lid, and, having introduced the liquid, seal the cover hermetically by moistening the edges in a drop of water spread on a pill-tile, before slipping it over the capsule; a mere trace of water being sufficient to cause a union between the cover and the capsule, any excess of moisture must be shaken off, as it would cause the capsule to soften and finally leak.

The well-known French pearls of ether, apiol, chloroform, etc., are gelatin globules filled with the respective liquids. According to Thévenot, they are prepared as follows: A mass composed of gelatin, acacia, sugar, and honey, is rolled into thin sheets, one of which, while still soft, is placed upon an iron plate of 6 millimeters (about ¼ inch) thickness, and containing numerous suitable cavities of 10 millimeters (about ⅜ inch) diameter, into which the mass sinks by reason of its weight, thus forming a hollow hemisphere in each cavity; the desired liquid is introduced by means of a pipette or small syringe, and a cover consisting of another sheet of the same gelatin mass is laid on. A second iron plate, corresponding exactly to the one first used, is now placed over the last sheet, and after screwing the plates together their position is reversed so that the second gelatin sheet may fill the cavities in the second iron plate, thus completing the spherical shape of the pearls or globules, which are finally separated from each other by subjecting the whole arrangement to powerful pressure.

Another method is said to consist in filling a tube, made of gelatin composition, with the respective liquids, and then, by means of a specially constructed machine, cutting off pieces of the required size and simultaneously pressing these into the proper shape. The apparatus used for this method is known as Viel's capsulator.

Pills are sometimes coated with collodion or balsam of tolu; the latter plan is directed in the official formulas for pills of iodide of iron and of phosphorus. To coat pills with collodion, they are simply impaled on needles and dipped into collodion, which is then allowed to dry; if water be present in the pills, the coating will become mottled or opaque. The Pharmacopœia directs a solution of 10 Gm. of balsam of tolu in 15 Cc. of ether, for coating pills, but, owing to the very rapid evaporation of the solvent, the process is unsatisfactory, as the pills are prone to stick. The following improvement by Dunning has met with considerable success: Dissolve 5 Gm. of balsam of tolu in 15 Cc. of alcohol with aid of a gentle heat; strain, and when cold add 5 Cc. of ether. Enough of this solution is poured into the lid of an 8-ounce ointment jar to form a thin layer, the pills are added, and the lid rotated until they are completely coated. The pills are then transferred to another lid, previously coated with liquid petrolatum by spreading one drop over the surface with the finger, and rotated for a few minutes to remove the excess of the tolu solution. They are finally placed in a third lid, coated like the second, and rotated until dry.

The so-called "pearl-coating" is applied in a manner similar to that used for gilding or silvering; the pills having been evenly dampened with a very thin adhesive liquid (mucilage of acacia ℥j, syrup ℥j, and water ʒvj, or tragacanth 4 grains, syrup ʒss, and water ʒviiss), are rotated in a globular box with purified talcum or a mixture of talcum and sugar in the form of an impalpable powder. If a high polish is desired, this can be obtained by rotating them afterward in another globe coated on the inside with paraffin.

Keratin coating has been especially recommended for pills which are not to be acted upon in the stomach, but to be dissolved in the intestinal fluids. Keratinized pills were first introduced by Dr. Unna, of Germany, but have not met with much favor, on account of the tedious process of coating. Keratin is a constituent of all horny matter, and is obtained from the same, after removal of fat with ether, by digestion, in the form of shavings or turnings with a mixture of pepsin, hydrochloric acid, and water, for twenty-four or thirty-six hours: this treatment removes all matter soluble in the gastric juice. The residue, having been well washed with water, is digested with 8 or 10 times its weight of 5 per cent. ammonia water in a loosely stopped flask, at a moderate heat, until a nearly complete solution results, which is then filtered and evaporated to dryness. Keratin, as thus prepared, is a commercial article; both acid and alkaline solutions of it are used for coating pills.

Ammoniacal solution of keratin is prepared by dissolving 7 parts of keratin in a mixture of 50 parts of 10 per cent. ammonia-water and 50 parts of 60 per cent. alcohol (solution may be facilitated by warming). This alkaline solution should be used for pills containing trypsin, pancreatin, metallic sulphides, etc.

Acetic solution of keratin, made by dissolving 7 parts of keratin in 100 parts of glacial acetic acid (if necessary, by the aid of a moderate heat), is adapted for pills containing ferric chloride, tannin, salicylic acid, arsenic, creosote, and the salts of mercury, gold, and silver.

For chemically indifferent substances, either the alkaline or acid solution of keratin may be employed.

All pills intended to be coated with keratin must be made with some fatty excipient and contain no appreciable moisture; the mass is best made with cacao butter and oil of sweet almond, or a mixture of purified mutton tallow or cacao butter 10 parts and white or yellow wax 1 part. After the pills have been rounded they should be dipped in melted cacao butter, which is allowed to harden; they are then placed in a porcelain dish, the keratin solution added (about 30 or 40 drops for 100 pills of medium size) and rotated until the pills have become thoroughly moistened, after which they are dried on parchment paper, to which they will not adhere. The application of keratin solution must be repeated three or four times and allowed to dry each time.

The above process is tedious, and in the majority of cases the following shorter method, proposed by Dunning, will be found entirely satisfactory: 1 Gm. of keratin is rubbed to a smooth paste with 6 Cc. of official spirit of ammonia and warmed, while a few drops of water, sufficient to produce a clear solution, are added. The pills do not require a coating of cacao butter, and having been made hard and dry are placed on the points of fine needles, and immersed one at a time in the solution, which is kept warm, the loss by evaporation being made up by addition of spirit of ammonia and a little water. After immersion in the solution, the pill is held in such a position that the drop forming on the under surface may be removed by a piece of card-board, after which the needle is rotated for a few moments and then pushed through a piece of card-board standing vertically, for the purpose of drying the pills. The minute orifice left by the needle-point is subsequently closed with a little of the keratin solution. This plan is especially adapted to a small number of pills, 12 to 30, at the dispensing counter.

Phenyl salicylate, or salol, being, like keratin, insoluble in the gastric juice, has also been recommended for coating pills not to be dissolved or disintegrated until the bowels are reached. In order to be efficient 3 separate coatings of salol are usually applied. A sufficient quantity of salol, 10 grains for 30 grains of pill-mass, having been melted in a dish on a water-bath, is cooled just short of congealing, when the pills are added and the dish rapidly rotated. The second coating requires about the same quantity of salol, which is also fused and applied a little warmer than the first. Lastly, a smaller quantity of salol, about two-thirds of the first quantity, is used in the same manner. Finally, in order to produce a smooth finish the pills are rapidly rotated in another portion of salol, about 3 grains for 20 three-grain pills, fused and applied while quite warm, the rotation being continued until the pills are cold.

THE OFFICIAL PILLS.

The U. S. Pharmacopœia gives working formulas for 14 varieties of pill-masses, and as these are directed to be divided into a definite number of pills, they are indicated under the title "Pilulæ." The term "Massa" is applied to those combinations which are intended to be kept on hand in bulk, being frequently prescribed as constituents of other pill-masses. In the British Pharmacopœia 20 formulas for pill-masses are given, but in no case is the mass directed to be divided into a given number of parts; they are all designated by the simple title "Pilula."

Alphabetical List of the Official Pills.

Latin Name.	English Name.	Composition of each Pill.	
Pilulæ:			
Aloes	Pills of Aloes	Purified Aloes	0.13 Gm.
		Soap	0.13 "
		Water a sufficient quantity.	
Aloes et Ferri	Pills of Aloes and Iron	Purified Aloes	0.07 Gm.
		Dried Sulphate of Iron	0.07 "
		Aromatic Powder	0.07 "
		Confection of Rose a sufficient quantity.	
Aloes et Mastiches	Pills of Aloes and Mastic	Purified Aloes	0.13 Gm.
		Mastic	0.04 "
		Red Rose	0.03 "
		Diluted Alcohol a sufficient quantity.	
Aloes et Myrrhæ	Pills of Aloes and Myrrh	Purified Aloes	0.13 Gm.
		Myrrh	0.06 "
		Aromatic Powder	0.04 "
		Syrup a sufficient quantity.	
Asafœtidæ	Pills of Asafetida	Asafetida	0.20 Gm.
		Soap	0.06 "
		Water a sufficient quantity.	
Catharticæ Compositæ	Compound Cathartic Pills	Comp'd Extract of Colocynth	0.08 Gm.
		Mild Mercurous Chloride	0.06 "
		Resin of Jalap	0.02 "
		Gamboge	0.015 "
		Diluted Alcohol a sufficient quantity.	
Catharticæ Vegetabiles	Vegetable Cathartic Pills	Comp'd Extract of Colocynth	0.06 Gm.
		Extract of Hyoscyamus	0.03 "
		" " Leptandra	0.015 "
		Resin of Podophyllum	0.015 "
		" " Jalap	0.02 "
		Oil of Peppermint	0.008 Cc.
		Diluted Alcohol a sufficient quantity.	

Latin Name.	English Name.	Composition of each Pill.		
Pilulæ:				
Ferri Carbonatis	Pills of Ferrous Carbonate (Ferruginous Pills) (Chalbeate Pills)	Ferrous Sulphate, crystalliz'd	0.16	Gm.
		Potassium Carbonate	0.08	"
		Sugar	0.04	"
		Tragacanth	0.01	"
		Althæa	0.01	"
		Glycerin and Water a sufficient quantity.		
Ferri Iodidi	Pills of Ferrous Iodide	Reduced Iron	0.04	Gm.
		Iodine	0.05	"
		Glycyrrhiza	0.04	"
		Sugar	0.04	"
		Extract of Glycyrrhiza	0.01	"
		Acacia	0.01	"
		Water a sufficient quantity.		
Laxativæ Compositæ	Compound Laxative Pills	Aloin	0.013	Gm.
		Strychnine	0.0005	"
		Ext't of Belladonna Leaves	0.008	"
		Ipecac	0.004	"
		Glycyrrhiza	0.046	"
		Syrup a sufficient quantity.		
Opii	Pills of Opium	Powdered Opium	0.065	Gm.
		Soap	0.02	"
		Water a sufficient quantity.		
Phosphori	Pills of Phosphorus	Phosphorus	0.0006	Gm.
		Althæa	0.060	"
		Acacia	0.060	"
		Glycerin and Water a sufficient quantity.		
Podophylli, Belladonnæ et Capsici	Pills of Podophyllum, Belladonna, and Capsicum	Resin of Podophyllum	0.016	Gm.
		Ext't of Belladonna Leaves	0.008	"
		Capsicum	0.032	"
		Sugar of Milk	0.065	"
		Acacia	0.016	"
		Glycerin and Syrup a sufficient quantity.		
Rhei Compositæ	Compound Pills of Rhubarb	Rhubarb	0.13	Gm.
		Purified Aloes	0.10	"
		Myrrh	0.06	"
		Oil of Peppermint	0.005	Cc.
		Water a sufficient quantity.		

Special Remarks.

If it is desired to keep any of the official pills in stock in an uncoated condition, they should at once be placed in a mixture of lycopodium and powdered licorice root, and allowed to remain there until dry, which may require from four to eight days; they can then be kept in bottles without danger of moulding or losing their shape. This plan is particularly advisable for the Compound and Vegetable Cathartic Pills.

The official Pills of Aloes, of Asafetida, and of Opium are so simple in composition as to require no special comment. On account of the soap present, the addition of water must be made cautiously, as an excess will render the mass too soft and unmanageable.

Pills of Aloes and Iron.—The excipient for these pills, directed by the Pharmacopœia, unless recently made, is likely to add considerably to the bulk of the mass, and hence a little honey should be added at the same time, which is preferable to either water or syrup and dries less rapidly.

Pills of Aloes and Mastic.—These pills, commonly known as Lady Webster Dinner Pills, are prone to become very hard in time; hence it appears preferable either to make them up fresh when wanted or to use a mixture of syrup and water equal parts, or glycerin and water equal parts, in place of diluted alcohol as an excipient. The mastic must be used in fine powder, and the three powders should be well mixed before any excipient is added.

Compound Cathartic Pills.—In making these well-known pills powdered resin of jalap is to be preferred to the pilular extract formerly directed; it should first be mixed with the gamboge and calomel, and finally with the powdered compound extract of colocynth. A moderate quantity of water (f℥vj for 1000 pills), which should be added to the mixed powders all at once, suffices to make a satisfactory firm mass, provided the mixture be well kneaded in the mortar. Compound Cathartic Pills should never be put into stock bottles until perfectly dry and hard.

Vegetable Cathartic Pills.—If the official directions are carefully followed, a satisfactory pill-mass will be obtained, the softened extract of hyoscyamus supplying the necessary moisture. As in the case of compound cathartic pills, the pilular extract of jalap, no longer officially recognized, has been replaced by resin of jalap.

Pills of Ferrous Carbonate.—Blaud's pills, as the official pills of ferrous carbonate are more commonly termed, have probably caused inexperienced pharmacists more trouble than any other pill-mass; this is partly owing to the fact that physicians frequently order equal parts of ferrous sulphate and potassium carbonate, which render the mass very deliquescent, on account of the excess of potassium carbonate. The official directions are to triturate the iron salt and sugar together, and add this mixture to the potassium carbonate previously rubbed smooth with glycerin and water (10 drops of each for every 100 pills); the mass is thoroughly triturated until it assumes a green color, and is then incorporated with the tragacanth and althæa, a little more water being added if necessary. The formula yields satisfactory results, the secret of success lying in the completed reaction between the iron and potassium salts before the final massing with tragacanth and althæa. The mass should be rolled out and cut while still moderately soft. The official formula is based on the assumption that absolutely pure potassium carbonate will be used, in which case the decomposition will be complete, as the 16 Gm. of crystallized ferrous sulphate require 7.954 Gm. of potassium carbonate, yielding 6.673 Gm. of ferrous carbonate; if the potassium carbonate used be less than 100 per cent. pure, an excess of ferrous sulphate will be present.

Mr. H. B. Dunning, of Baltimore, has suggested the following modification of the pharmacopœial formula, which eliminates the tragacanth and althæa, as these have a tendency to make the pills tough and hard. Take of Ferrous Sulphate crystals 15 Gm., Potassium Carbonate 8.75 Gm., Sugar 1.25 Gm., Powdered Glycyrrhiza 6.25 Gm. Rub the iron and sugar into fine powder, add the potassium carbonate previously powdered, and mix with 40 minims of water. Triturate the mixture until dry and in powder, add the glycyrrhiza and sufficient glucose to make a smooth mass, which divide into 100 pills. Pills made by this formula retain their shape and green color for a long time (over three months in paper boxes), and while assuming a darker color on the outside, due to gradual drying, the interior remains fairly soft.

Physicians sometimes prescribe 4 drachms each of ferrous sulphate and potassium carbonate to be made into 100 pills, which proportions should be changed to 4 drachms and 140 grains, respectively. In such cases the following method of procedure has been used with marked success for many years: Rub the 240 grains of crystallized ferrous sulphate into a fine powder with 30 grains of sugar, and mix with 140 grains of potassium carbonate also reduced to powder; the mixture, which will soon soften and change color, should be stirred from time to time until the reaction is complete, which is known by the disappearance of the granular condition and the formation of a green, smooth, very soft paste. Now add 30 grains each of powdered starch and powdered acacia, mass quickly, and roll out while still soft, as the mass rapidly becomes firm, and may then crumble when rolled out.

Blaud's pills are intended to contain about 0.0667 Gm. (about 1 grain) of ferrous carbonate, and cannot be kept on hand uncoated on account of the tendency to rapid oxidation of the iron salt, which is retarded, but not entirely obviated, by the sugar or sugar and glycerin present. The pills should be of a uniform deep-green color, and are best prepared fresh when wanted. In Great Britain the mass for Blaud's pills is officially recognized by the simple term "Pilula Ferri," and its composition is about the same as that published in our own Pharmacopœia.

Pills of Ferrous Iodide.—The first step in the manufacture of pills of ferrous iodide is to mix the reduced iron with water (6 Cc. for 100 pills), then adding the iodine, and stirring until the reddish tint of the mixture disappears. The glycyrrhiza, acacia, and sugar are now added, and after thorough admixture the whole is evaporated on a water-bath to a pilular consistence. The official pills are presumably identical with Blancard's Pills; they contain an excess of iron, which aids in their preservation. Each pill is designed to contain about 0.0610 Gm. (about 1 grain) of ferrous iodide. Owing to the heat generated by the union of the iodine with the finely divided iron, the former should be added slowly, so as to avoid loss by vaporization, and the mixed powders should not be added until all traces of free iodine have disappeared. When the mass has been evaporated to a proper consistence on a water-bath it will weigh about 20 Gm. The 5 Gm. of iodine ordered in the official formula require 1.104 Gm. of absolutely pure iron to form ferrous iodide; the amount of iron in excess will, therefore, depend upon the purity of the reduced iron used.

Since pills of ferrous iodide are not, as a rule, made extemporaneously, and are readily affected by air and moisture, the Pharmacopœia very properly directs a resinous coating to be applied; a modified form of tolu solution, which has been found preferable to the official ethereal solution, has already been referred to on page 361.

Pills of Phosphorus.—The official directions for making pills of phosphorus are to dissolve the carefully weighed phosphorus in chloroform (5 Cc. for 100 pills) contained in a test-tube, heating gently if necessary to facilitate solution. Mix the althæa and acacia, add the solution of phosphorus, then immediately afterward a mixture of glycerin 2 volumes and water 1 volume (4 Cc. for 100 pills), and quickly form the mass. The uniform distribution of phosphorus in a pill-mass is best effected in a state of solution, and the choice of chloroform as a solvent in the official formula has a double advantage. Chloroform, besides being one of the best solvents for phosphorus known, is readily dissipated, owing to its very volatile nature, leaving the phosphorus, in a very finely divided form, intimately distributed throughout the mixed powders, while its heavy, non-inflammable vapor hovers over the mortar during the making of the pill-mass, thus protecting the phosphorus against oxidation. Phosphorus, being very inflammable, must be cut and weighed under water, hence the weighing of small quantities is often attended with much difficulty. A small glass capsule or a watch-crystal, containing some water, should be carefully tared, and in it the phosphorus, having been cut into small pieces under water with a penknife, should be weighed; the pieces may be removed with a small pair of forceps, quickly dried by means of filter-paper, and then dropped into the chloroform contained in a test-tube.

Phosphorus is rapidly oxidized, particularly in a state of fine division; hence pills of phosphorus should be coated as soon after they have been made as possible; as in the case of pills of ferrous iodide, the modified solution of balsam of tolu is preferable to the official ethereal solution.

The official method for incorporating phosphorus in a pill-mass may also be followed when phosphorus is ordered in combination with other remedial agents, such as quinine sulphate, extract of nux vomica, etc. If phosphorus be extensively used in pill form, another plan is to prepare a 10 per cent. intimate mixture of phosphorus and rosin, as follows: Weigh off 1 Gm. of phosphorus and melt the same by placing it in a mortar containing hot water (not boiling); now add 9 Gm. of rosin, which softens in the hot water, and mix the phosphorus and rosin *intimately* by triturating and kneading. Pour off the water and preserve the phosphoretted resin, after it has been dried between filter-paper, in a small, tightly stoppered bottle in a dark place. Each gramme of this preparation represents 0.100 Gm. of phosphorus, or 10 grains equal 1 grain, and may be conveniently weighed without danger of ignition. It keeps well for some time, but gradually the phosphorus becomes oxidized, the change beginning on the exterior and slowly extending inward.

Compound Pills of Rhubarb.—Compound pills of rhubarb will become very hard by age, and as they are not often called for, it is decidedly better to keep the ingredients properly mixed, in a glass-stoppered bottle, and make the mass when required. A mixture of syrup and water, or glycerin and water, may be used with advantage in place of water, as in the case of pills of aloes and mastic.

THE OFFICIAL MASSES.

As stated before, these masses are usually employed as constituents of other pill-masses; they are Massa Ferri Carbonatis and Massa Hydrargyri. The latter only is of sufficiently firm consistence to admit of being rolled into pills which will retain their spherical shape without the addition of absorbents, except when freshly made in warm weather.

Mass of Ferrous Carbonate, or Vallet's Mass, is a mixture of ferrous carbonate, sugar, and honey. Even when very carefully made, so as to contain the full amount of iron salt, it is never of a pilular consistence, but always in the form of a rather tenacious paste. The Pharmacopœia directs the preparation of ferrous carbonate by mixing cooled and filtered solutions of ferrous sulphate and sodium carbonate, made respectively with crystallized ferrous sulphate 100 Gm., boiling distilled water 200 Cc. and syrup 20 Cc., and monohydrated sodium carbonate 46 Gm. and boiling distilled water 200 Cc., and then washing the resulting precipitate well with sweetened water (syrup 1 volume, distilled water 19 volumes) until the newly formed sodium sulphate has been removed; the washing is best performed by decantation in flasks having a narrow neck, and which can be tightly stoppered. The precipitate is then drained on a strainer, mixed with clarified honey 38 Gm. and sugar 20 Gm., and the whole evaporated in a tared capsule, with constant stirring, until reduced in weight to 100 Gm.

The iron solution should be poured slowly into the alkaline solution and the flask frequently rotated as long as carbon dioxide escapes, after which it is filled with distilled water, corked, and set aside. The object of adding syrup to the iron solution, and of the subsequent washing of the precipitate with sweetened water, is to prevent oxidation of the iron salt as far as possible. Instead of distilled water, pure river or spring water recently boiled may be used throughout the process.

Theoretically the official product should contain about 42 per cent. of ferrous carbonate, as 100 Gm. of crystallized ferrous sulphate will yield 42 Gm. of the carbonate, but as there is always some loss during the washing process, the finished mass rarely contains more than 36 per cent., and this much only if care has been observed to prevent oxidation by rigid exclusion of air. Freshly precipitated ferrous carbonate is greenish gray, gradually deepening in color, and the finished mass is decidedly green, but should not be brown, which would indicate oxidation. When Vallet's mass is allowed to stand for some time, even in well-covered jars, it becomes dry on the surface and assumes a blackish-green color. The change extends to the interior very slowly, being due to the gradual escape of moisture.

Mass of Mercury, better known as Blue Mass or Blue Pill, is probably the most familiar of all pill-masses. In the official formula 33 parts of mercury are triturated with a mixture of 9 parts of glycerin and 33 parts of honey of rose, until extinguished, the viscid character of the vehicle enabling a rapid division into minute globules. When mercury is no longer visible to the naked eye, and the mixture has assumed a uniform brownish-gray appearance, 10 parts of powdered licorice root and 15 parts of powdered althæa are gradually added with constant trituration, until the mercury is so finely divided that it cannot be detected with a lens of at least 10 diameters magnifying power. Blue mass contains 33 per cent. of metallic mercury, which probably undergoes slight superficial oxidation in the course of time, but is well protected by the other ingredients.

CHAPTER XXIX.

CONFECTIONS AND LOZENGES.

CONFECTIONS.

THIS class of medicinal preparations still finds recognition in the leading pharmacopœias, although, in this country at least, they are very rarely used by physicians. At one time the incorporation of saline and vegetable remedial agents with honey or fruit-pulp was a favorite mode of medication, such being the invariable composition of electuaries or confections, which were dispensed in the form of a thick, semifluid mass. When made with honey, or with the addition of glycerin, confections retain their original soft condition for a long time; but if made with fruit-pulp, or sugar and water, the moisture gradually evaporates and the mass becomes dry and hard. All medicinal ingredients must be added in the form of impalpable powder, and heavy metallic salts should never be employed, as they are prone to sink to the bottom and thus become separated. Whenever essential oils are to be incorporated in confections, they should first be triturated thoroughly with some finely powdered sugar; narcotic extracts or other potent remedies should be added in the form of solution, so as to insure their uniform distribution throughout the soft mass.

The U. S. Pharmacopœia at present recognizes but 2 confections, and the German Pharmacopœia 1—*Electuarium Sennæ;* while the British Pharmacopœia still retains 4—*confection of pepper, roses, senna*, and *sulphur*.

The Official Confections.

Confectio Rosæ.—Confection of rose, which at one time was largely used as a favorite excipient for certain pill-masses, possesses little or no medicinal virtue. It is made by rubbing 80 Gm. of red rose leaves, in No. 60 powder, with 160 Cc. of stronger rose water, previously heated to 65° C. (149° F.), for the purpose of reducing the rose petals to a pulpy condition, and then gradually adding 120 Gm. of clarified honey and 640 Gm. of finely powdered sugar.

Confectio Sennæ.—Confection of senna, sometimes called for under the name of lenitive electuary, if carefully prepared, presents an agreeable, mild laxative preparation. The Pharmacopœia directs that 100 Gm. of tamarind, 70 Gm. of prune, 120 Gm. of fig, and

160 Gm. of cassia fistula be digested with 500 Cc. of water for three hours on a water-bath. The coarser portions are then to be separated with the hand and the pulpy mass rubbed first through a coarse hair sieve, and then through a fine one or through a muslin cloth. This treatment with the hands is objectionable, and by no means necessary, for if the digestion be carried on on a boiling water-bath for three hours, with occasional stirring by means of a thick glass rod or a porcelain spatula, the pulpy mixture can easily be passed through a hair sieve with the aid of a horn spatula. The residue remaining in the sieve is again digested for a short time with 150 Cc. of water, the mixture treated as before, and the product added to the pulpy mass first obtained. In the pulpy liquid 555 Gm. of sugar are dissolved and the whole evaporated to 895 Gm., to which while yet warm are added 100 Gm. of senna, in No. 60 powder, and 5 Gm. of oil of coriander. It will be found advisable, instead of adding the oil directly with the senna to the pulp, to triturate it thoroughly first with about 50 Gm. of sugar, which should be reserved for that purpose out of the original quantity.

LOZENGES OR TROCHES.

Lozenges are solid, flattened masses of round, oval, or other desirable shape, not intended for mastication, but to be dissolved slowly in the mouth, therefore not adapted for medicines which are expected to undergo disintegration in the stomach prior to any therapeutic action. In one or two cases the cylindrical form is preferred, as for the well-known licorice lozenges and Wistar's cough lozenges. The remedial action of lozenges is generally designed to be purely local, either as an expectorant, demulcent, stimulant, sedative, astringent, or antiseptic.

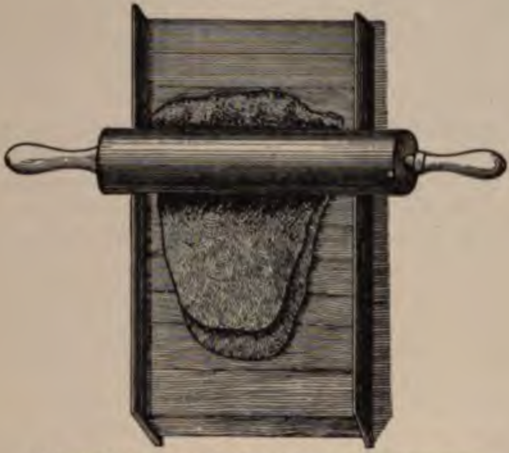
The usual base or vehicle for lozenges is sugar (that known among confectioners as lozenge sugar being preferred), although powdered extract of licorice also is added at times, and, of late years, fruit paste, made from black or red currants, has come extensively into use for certain kinds of lozenges. Adhesiveness is obtained by the addition of tragacanth or acacia, and syrup or water (plain or aromatic) is used to supply the necessary moisture. All medicinal constituents, as well as the sugar or extract of licorice should be in very fine powder to insure a smooth paste, and potent remedies, wherever possible, should be added either in the form of solution or triturated with a small quantity of sugar before being mixed with the other ingredients, so as to insure uniform distribution. Tragacanth is preferable to acacia for making a lozenge-mass, as the resulting paste is more tenacious; in both cases the mucilage is to be preferred to the powder with the subsequent addition of water, as in the latter case it is often difficult to avoid an excess of moisture, which retards subsequent drying.

The British Pharmacopœia (1898) admits acacia only as the adhesive agent for lozenges, and designates four distinct bases or vehicles of the following composition: *Simple basis*—sugar 496 Gm., powdered acacia 19.5 Gm., mucilage of acacia 35.5 Cc., water a sufficient quantity. *Fruit basis*—sugar 439.5 Gm., powdered acacia 19.5 Gm., mucilage of acacia 35.5 Cc., black-currant paste 56.75 Gm., water a sufficient quantity. *Rose basis*—sugar 496 Gm., powdered acacia 19.5 Gm., mucilage of acacia 17.5 Cc., rose water a sufficient quantity. *Tolu basis*—sugar 482 Gm., powdered acacia 19.5 Gm., mucilage of acacia 35.5 Cc., tincture of tolu 10.5 Cc., water a sufficient quantity. Instead of giving individual formulas for making the 17 varieties of lozenges recognized, a general formula, adjusted for 500 lozenges, is given under the head of each basis, as follows: 500 times the quantity of medicinal agent required for one lozenge is intimately mixed with the sugar and acacia, and a paste then made with the other ingredients, which is divided into 500 equal parts and dried at a moderate temperature.

Lozenge-masses are made after the manner of pill-masses, except that more adhesive material is used, and the paste is made somewhat softer. The proportion of powdered tragacanth necessary for a well-made plastic mass may vary from 1 to 3 per cent. of the total weight of the mixed powders (acacia about three or four times as much); and in making the mass the necessary water or syrup should be added cautiously, and the mixture well kneaded after each addition, so as to avoid too soft a condition, which readily occurs on account of the great solubility of the sugar. A good plan is to follow the suggestion of Hager, to reserve about one-fifth of the powder, and when the remaining four-fifths have been made into a plastic mass, quickly incorporate the reserve portion, which can be done without risk of the mass becoming dry and crumbly. For massing small quantities of material a Wedgewood mortar and pestle will be found quite convenient, while for large quantities the pill-mass mixers shown on page 345 are preferable.

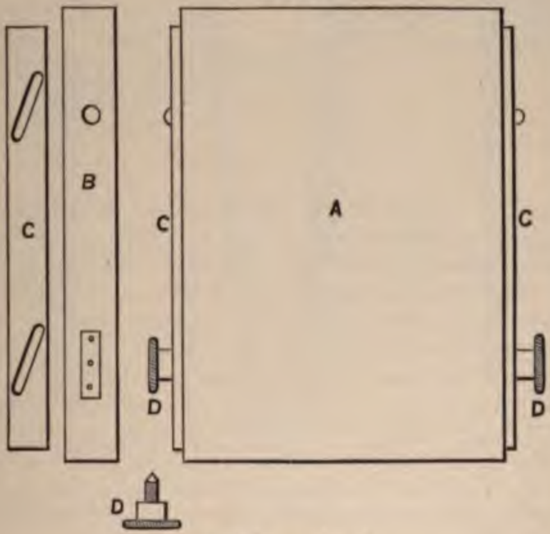
After a suitable mass has been made, it is transferred to a hardwood board or a stone slab, rolled out into either a flat sheet or a cylinder, and divided into the requisite number of parts. When cylindrical lozenges are to be made, the mass is rolled out without dusting and divided into pieces about five-eighths of an inch in length, by means of a special cutter. In order to prevent the mass from adhering the flat roller may be lightly rubbed with a very small quantity of oil of sweet almond. For flat lozenges the mass is conveniently rolled out into a sheet, the required thickness of which must be ascertained by experiment; this is done by dividing the weight of the whole mass by the number of lozenges to be made, then weighing off as many grains of the mass as correspond to the quotient obtained, and forming this into a lozenge by means of a punch or spatula. As every well-made lozenge-board is provided with guides and screws for regulating different thicknesses, no difficulty will be experienced in adjusting the side strips to the proper height, and then rolling out the mass by means of a cylindrical roller, as shown in Fig. 239. To prevent adhesion of the mass, the oard may be dusted with a little starch or a mixture of starch and ugar.

Fig. 239.



Showing the manner of rolling out the lozenge-mass.

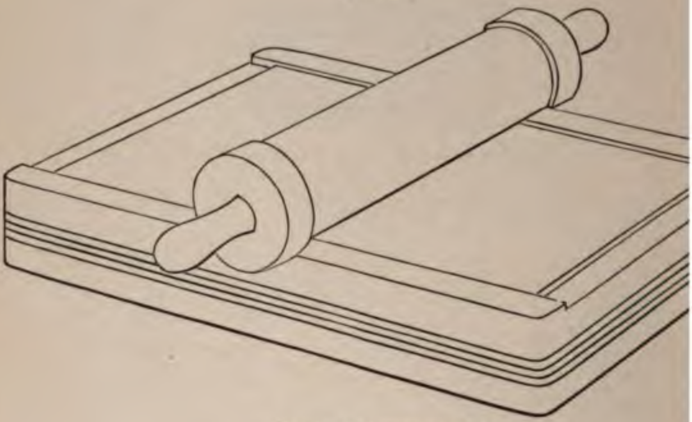
Fig. 240.



Procter's lozenge-board.

The lozenge-board lately designed by Wallace Procter is very useful and simple in construction, as shown in Fig. 240. A is a board of well-seasoned hard wood, $1\frac{1}{2}$ inches thick, 10 inch and 14 inches long, planed perfectly flat, and both sides and en square and true. At each side, about 3 inches from one enc is let in flush and tapped with a screw, as shown in B. side of the board a plate of brass, $1\frac{1}{2}$ inches wide, 14 inch and $\frac{3}{16}$ of an inch thick, is fitted. Each plate has two slots it diagonally (see C) $\frac{3}{8}$ of an inch from each edge; these slo have exactly the same slope, and the front slot should be divisions of $\frac{1}{32}$ of an inch. Through one slot of each square-shouldered screw passes, and is screwed in until it pr plate close to the side of the board, but still permits it easily; through the other slot in each plate passes a set-screw enters the screw-plate before mentioned. When the plat

Fig. 241.

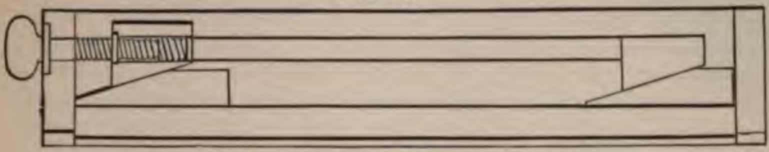


Harrison's lozenge-board.

been adjusted to a given height the set-screws are turned u prevent motion of the plate.

Harrison's lozenge-board (see Fig. 241), which has bee for many years, consists of two frames of wood, of which on forward and backward inside of the other in grooves cut outer frame; the board on which the mass is rolled rests fi the inner frame, and has fastened to its bottom two bevelle corresponding to similar strips attached to the frame. By n a screw the inner frame can be pushed forward, and the bo forced upward (see Fig. 242). As the bevels give $\frac{3}{8}$ of an i for which 15 complete revolutions of the screw are requir half-turn of the screw will cause a rise of $\frac{1}{80}$ of an inch; in any required thickness of the mass can be obtained. The out is stationary, the sides projecting $\frac{3}{8}$ of an inch above the e serving as a support for the rolling-pin, which is also provi a flange at each end to keep it in proper position. While the pins are usually made of wood, steel or glass rollers may also be used, the former being particularly desirable when heat is to be employed.

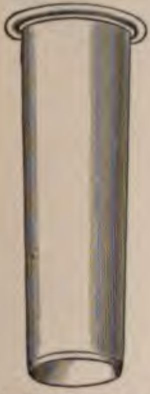
FIG. 242.



Harrison's lozenge-board (sectional view).

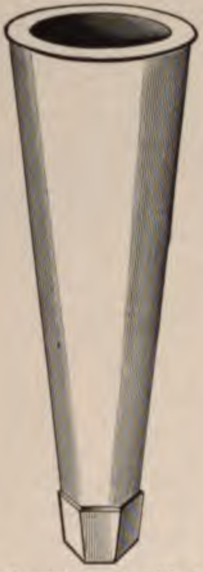
The punches used for cutting lozenges are usually in the form of tapering cylinders made of heavily tinned iron, and frequently provided with sharp cutters of hardened steel, the shape of which varies with the fancy of the operator; sometimes they are made with straight sides and fitted with a plunger, operated by a spring, for the ready expulsion of the lozenges. Figs. 243, 244, and 245 represent some of the usual styles. In large manufacturing establishments ten or twelve cutters are frequently combined and operated as one, greatly expediting the work. Whenever it is desired to stamp lozenges with some special letter or design, this is done at the time of cutting them, the plunger being provided with the necessary die.

FIG. 243.



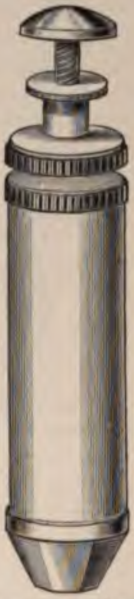
Plain tin lozenge-cutter.

FIG. 244.



Tin lozenge-punch with steel cutter.

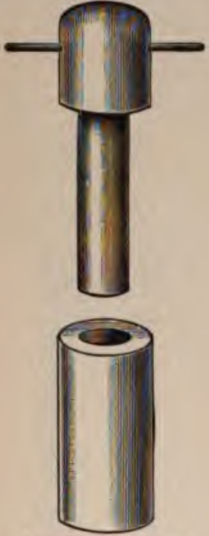
FIG. 245.



Lozenge-punch with spring.

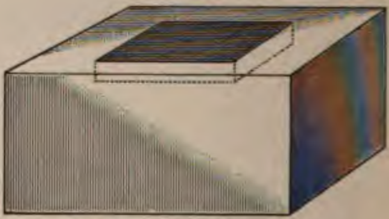
As the preparation of lozenges has almost entirely passed out of the hands of the retail pharmacist, very few stores are now provided with suitable appliances for making them. When a small number of lozenges is wanted extemporaneously, a stiff mass should be made in order to facilitate subsequent drying; it may then be rolled out on a pill-machine or pill-tile, to be cut into the requisite number of parts, each of which should be given a globular shape and then flattened into a suitable disk, for which purpose the simple apparatus shown in Fig. 246 will be found very convenient. This consists of a brass or steel tube, about 2 or 3 inches long, $\frac{3}{8}$ to $\frac{5}{8}$ of an inch in diameter, and of $\frac{1}{8}$ or $\frac{3}{16}$ of an inch in thickness; the bore of the tube must be uniform and smooth and the ends square, otherwise the lozenges will present an irregular appearance. A plunger accurately fitting the tube, preferably made of the same metal, is necessary; it should be of the same length as the tube, and provided with a top about an inch long, exactly covering the outside diameter of the tube. It is desirable that both parts be nickel-plated. To shape the lozenges properly, the globular mass, slightly dusted with starch and sugar or lycopodium, is placed in the cylinder, resting upon a metallic base, which consists of a nickel-plated piece of steel or brass, about 2 inches square and $\frac{1}{4}$ inch thick, set in a block of hard wood (see Fig. 247); the plunger having been inserted, it is struck a quick, sharp blow with a mallet, after which the cylinder is raised and the lozenge expelled by slightly tapping the plunger with the mallet. The apparatus shown on page 384, Fig. 248, may also

FIG. 246.



Lozenge apparatus.

FIG. 247.



Base for lozenge apparatus.

be employed for shaping lozenges, although it is inferior to the above for compressing masses, owing to the projection of the base into the cylinder.

Gelatin lozenges, variously medicated, have been in use for some time, more particularly in Europe. They are composed of a mixture of gelatin, glycerin, and water, holding the medicinal ingredients either in solution or simple admixture. The base is often termed glyco-gelatin, and is made by macerating gelatin with water on a water-bath, and then adding glycerin; two kinds, containing different proportions of gelatin and glycerin, are in use. A mixture of gelatin, 1 ounce; orange-flower water, 2½ ounces; and glycerin, 2½ ounces (by weight), yields the softer variety, which is very readily soluble in the mouth; whereas a mixture of gelatin, 5 ounces; orange-flower water, 6 ounces; and glycerin, 6 ounces (by weight), evaporated to 15 ounces, produces a much firmer mass, dissolving more slowly, but probably better adapted for stock lozenges in this latitude; in the latter case at least twelve hours' maceration should be given the gelatin and water before adding the glycerin and applying heat. Gelatin lozenges must always be made with the aid of heat, and the mass after thorough admixture with the medicinal ingredients, while still in a melted condition, is poured into suitable moulds, where it rapidly congeals. A very convenient mould for a small number of the lozenges is found in the two side plates of the Konseal filling apparatus shown on page 404. If either of these plates be laid upon a cold porcelain or glass plate, the mixture may be poured directly into the particular perforations selected, and when cold the lozenges are easily removed by being pushed through the perforations. The proper quantity of gelatin mass to use for any particular case is ascertained by filling the perforations with some of the melted plain mass, and when cold weighing the disk; by keeping a memorandum of the weight of such disks much annoyance and labor can be saved. Gelatin lozenges vary in weight from 0.3 to 1.0 Gm. (5 to 15 grains).

Gelatin lozenges, while admirably adapted for the exhibition of such substances as cocaine, boric acid, carbolic acid, etc., are unsuited for tannin, extract of rhatany, and other agents incompatible with gelatin.

Chocolate lozenges, also known as chocolate tablets and chocolate pastilles, or simply as chocolates, may be conveniently made at the dispensing-counter as follows: The medicinal ingredients are intimately mixed with powdered sugar previously flavored with vanilla, Ceylon cinnamon, peppermint, or other flavoring agent (see Oil-sugars), and the mixture then added to three-fourths of its weight of chocolate, in mass or powder, contained in a mortar or porcelain dish. By means of water-bath heat a soft mass is obtained, which is thoroughly mixed, and when cool divided into the requisite number of parts on a lozenge-board or a pill-tile. Chocolate lozenges vary in weight from 0.3 to 1.0 Gm. (5 to 15 grains), and are not intended to be dissolved slowly in the mouth, but to be swallowed with or without previous mastication.

Lozenges intended for immediate use do not require much drying, but those intended for stock must be thoroughly dried before they are put away in glass containers, otherwise they are liable to soften and adhere, and may even become mouldy. The drying is best effected on perforated trays in a moderately warm room. To avoid cracking of the edges, which will sometimes occur when lozenges are dried, the addition of a small quantity of glycerin to the water used will be found advantageous, and does not interfere with proper desiccation.

The average weight of lozenges is between 0.650 and 1.30 Gm. (10 and 20 grains), although in the nine working formulas of the Pharmacopœia the weight is found to vary between 0.40 and 0.96 Gm. (6 and 15 grains).

The following is a list of the official lozenges, showing the composition and excipient used:

TABLE OF OFFICIAL LOZENGES.

Latin Name.	English Name.	Composition of each Lozenge.
Trochisci:		
Acidi Tannici	Troches of Tannic Acid	Tannic Acid . . . . 0.060 Gm. Sugar . . . . 0.650 " Tragacanth . . . . 0.020 " Stronger Orange Flower Water a sufficient quantity.
Ammonii Chloridi	Troches of Ammonium Chloride	Ammonium Chloride . . . 0.100 Gm. Extract of Glycyrrhiza . . . 0.200 " Tragacanth . . . . 0.020 " Sugar . . . . 0.400 " Syrup of Tolu a sufficient quantity.
Cubebæ	Troches of Cubeb	Oleoresin of Cubeb . . . . 0.020 Gm. Oil of Sassafras . . . . . . 0.010 Cc. Extract of Glycyrrhiza . . . 0.250 Gm. Acacia . . . . 0.120 " Syrup of Tolu a sufficient quantity.
Gambir	Troches of Gambir (to replace the troches of catechu, formerly official)	Gambir . . . . 0.060 Gm. Sugar . . . . 0.650 " Tragacanth . . . . 0.020 " Stronger Orange Flower Water a sufficient quantity.
Glycyrrhizæ et Opii	Troches of Licorice and Opium	Extract of Glycyrrhiza . . . 0.150 Gm. Powdered Opium . . . . . 0.005 " Acacia . . . . 0.120 " Sugar . . . . 0.200 " Oil of Anise . . . . 0.002 Cc. Water a sufficient quantity.
Krameriæ	Troches of Krameria	Extract of Krameria . . . 0.060 Gm. Sugar . . . . 0.650 " Tragacanth . . . . 0.020 " Stronger Orange Flower Water a sufficient quantity.
Potassii Chloratis	Troches of Potassium Chlorate	Potassium Chlorate . . . . 0.150 Gm. Sugar . . . . 0.600 " Tragacanth . . . . 0.030 " Water a sufficient quantity.

Latin Name.	English Name.	Composition of each Lozenge.
Trochisci:		
Santonini	Troches of Santonin	Santonin . . . . 0.030 Gm. Sugar . . . . 0.900 " Tragacanth . . . . 0.030 " Stronger Orange Flower Water a sufficient quantity.
Sodii Bicarbonatis	Troches of Sodium Bicarbonate	Sodium Bicarbonate . . . . 0.180 Gm. Sugar . . . . 0.540 " Nutmeg . . . . 0.010 " Mucilage of Tragacanth a sufficient quantity.

CHAPTER XXX.

COMPRESSED TABLETS AND TABLET TRITURATES.

COMPRESSED TABLETS.

THIS class of remedies, allied to lozenges, under the name "compressed pills," was introduced into England nearly sixty years ago, and some years later into this country. The former name, although in a measure erroneously applied, because pills are understood to be made from a previously prepared plastic pill-mass, is still used by one or two manufacturers. Compressed tablets are lenticular-shaped disks containing one or more medicinal agents, and are obtained by compressing the material in the form of a granular powder into suitable shape by means of specially constructed apparatus operated by hand, steam, gas, or electric power.

Compressed tablets, although greatly in favor among physicians, for many years left much to be desired, and it is doubtful whether their extended use was justified, since the firm compression rendered many of them slowly soluble, while those containing insoluble substances failed to break up in water or the fluids of the stomach, even after hours of contact, so that the action of such tablets was either very much retarded or altogether prevented. Of late years, however, great improvements have been made in this respect, and compressed tablets are now made in such form that they will disintegrate within a few seconds when placed in water. This rapid and complete disintegration is especially desirable for such insoluble substances as bismuth subnitrate, bismuth subgallate, calcined magnesia, quinine sulphate, and various combinations of these with other substances. Its achievement must be admitted to be a decided and valuable improvement, and the process by which it is done is quite simple. The admixture of powdered starch with the granulated mixture as it is being fed into the compressor is known to impart to the tablet its disintegrating property, the exact quantity of starch necessary varying with different combinations. It is possible that manufacturers employ other agents in addition to starch, with a view to increasing the rapidity of disintegration of the tablets; but if so, such additions are not made public, and the secret is strictly guarded; plain starch, however, has been found very efficient. In addition to this improvement, the ready portability of compressed tablets, their convenient dosage, and comparative tastelessness when swallowed, together with their stability when properly made and kept, have at the present day increased their manufacture and use to an enormous extent. The fact that compressed tablets may be readily sugar-coated or chocolate-coated has also added much to their popularity. The variety of combinations of medicinal agents capable of being presented in this form is practically without limit. Nevertheless not all medicaments are suitable for preparation into compressed tablets. This is especially the case with very volatile or readily oxidizable substances, since in the necessary exposure of the material during its preparation for compression considerable loss by volatilization is likely to occur, as in the case of camphor, or the material is changed by oxidation, as in the case of phosphorus. For such substances a well-made pill properly protected by a coating is to be preferred.

It is manifestly impossible to give complete working directions for the preparation of every possible combination of remedial agents into compressed tablets, and much must be left to the judgment of the operator as each case presents itself. The general principles underlying this branch of pharmaceutical manipulations, however, are elucidated here. The first object must be to obtain the material to be compressed in the condition of a fairly uniform granular powder, a No. 20 or No. 30 granule being the usual degree of fineness employed. Fine powders are not adapted for compression, since the air which they carry with them when fed into the die is confined in the interstices between the particles, and cannot escape upward or downward during compression between the closely fitting dies and punches, hence imperfect compression results; moreover, fine powders have a tendency to cake or pack closely, and therefore do not feed regularly into the die. They also have a greater tendency to adhere to the surfaces of the punches and the sides of the die than does the same material in a granular form.

When the tablet to be compressed is to contain a single medicinal substance, this can often be bought in a granular form from the wholesale dealer, as, for instance, potassium chlorate, potassium, sodium, and ammonium iodides, bromides, and chlorides, potassium permanganate, sodium phosphate, zinc sulphate, etc. In such cases it is only necessary to reduce the commercial granular powder to a more uniform condition by passing it through a clean No. 20 iron sieve. No excipient whatever is necessary for these substances, although at times it may be necessary to subject the material to the action of dry, warm air for a short time, in order to free it from accidental moisture. When salts containing water of crystallization are to be compressed alone and require previous drying, care must be taken not to expel any of this water. Sometimes crystallized salts may be reduced to the proper granular condition by simply grinding them in a mill.

Greater difficulty is experienced and more care must be exercised when two or more substances, either all medicinal or part medicinal and part diluent or excipient, are to be mixed and granulated. In such cases all ingredients should be in the form of a fine powder. If potent remedies are to be incorporated, they should be thoroughly triturated either with the diluent or with the other ingredients, and the mixture should then be passed through a No. 80 bolting-cloth sieve, and again well mixed after sifting. The mixture is then moistened with whatever fluid or mixture of fluids the medicinal constituents or the diluents or excipients may dictate. The moistening fluid may be water, alcohol, a mixture of alcohol and water in various proportions, or aqueous solutions of glucose of different strengths. Glycerin should never be used, since it does not dry out and has a tendency to render the granules sluggish when feeding into the die. The fluid should be carefully and uniformly distributed through the entire mass, and in most instances only a sufficient quantity should be used to produce a well-moistened powder. This is then pressed through a No. 12 or No. 16 brass, iron, or tinned-iron wire sieve. The choice of the size and kind of sieve will depend on the physical and chemical properties of the material being operated upon, and these properties may render it necessary to omit the passing of the moist powder through a sieve altogether. This is the case when any constituent of the mixture is likely to be affected by the metallic surface of the sieve, as, for instance, the various mercurials, salicylates, etc. Sometimes also the components when moistened form too tough a mass to permit its being forced through a sieve. In such cases the material is dried out immediately after having been moistened, and is then ground in a mill or a mortar to the proper granular condition. The moistened powder which has been forced through a sieve is spread on glass plates or sized paper, and dried by exposure to either ordinary or warmed air. The physical and chemical properties of the substance will again dictate the conditions under which this drying should be conducted. Readily fusible (salol) or volatile (camphor, benzoic acid, essential oils, etc.) substances should be dried in the cold. When small quantities of volatile substances, as, for instance, flavoring oils, etc., are to be incorporated, they may be omitted from the mass and subsequently sprayed over the dried granules after having previously been dissolved in a little alcohol or ether. The granules should then again be carefully mixed. Most substances permit drying by means of circulating warm air, and all such as are readily affected by light should be carefully protected during drying. The dried granules are now forced through a No. 20 or No. 30 sieve. If during this operation much fine powder has been produced, it may be necessary to separate the same by means of a fine sieve and to regranulate it.

Sometimes it is necessary to add to the granular powder a lubricant, preferably the best quality of liquid petrolatum, in order to enable the tablet to be more readily expelled from the die. Usually about 1 fluidrachm of liquid petrolatum to 1 pound of granules is sufficient, it being dissolved in about an equal volume of ether and sprayed over the granules. In order to prevent the material from adhering to the punches, the granules may be dusted with a little finely powdered talcum or lycopodium, about $\frac{1}{4}$ ounce of the former or $\frac{1}{8}$ ounce of the latter to a pound. When tablets are to be used for preparing clear solutions, a little boric acid may be used in place of the talcum or lycopodium, provided the acid be not incompatible with the constituents of the tablet. Care must be taken not to crush the granules while the lubricants are being added.

When substances possessing no inherent adhesiveness are to be granulated, they require the addition of an excipient, such as acacia, sugar, tragacanth, or glucose, the first three in the form of fine powder, the latter in solution. Of all such substances, charcoal probably requires the largest proportion of excipients, from 5 to 10 per cent. of gum together with 15 or 20 per cent. of sugar or glucose being necessary; water is used as the moistening agent, and the mass must be well worked.

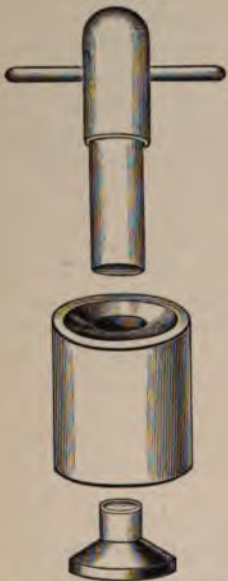
Tablets containing such sparingly soluble substances as acetanilid, phenacetin, salol, sulphonal, etc., are improved by the addition of a little starch.

Whenever tinctures or fluid extracts are to be administered in compressed tablet form, they are preferably evaporated with moderate heat over a water-bath to a syrupy consistence before they are mixed with the other ingredients; if no other diluent powder has been prescribed, the syrupy liquid may be incorporated with a mixture of finely powdered starch and sugar for the purpose of granulation. Solid extracts may be used either in the form of a vacuum-dried fine powder or the pilular extract may be softened with a little alcohol, alcohol and water, or water, as may be necessary. The softened extract is then incorporated with the diluent or other ingredients, which may necessitate working the mixture into a perfectly uniform pill-mass, to be then broken into small pieces and dried, and finally ground to the proper granular condition.

If tablets, upon solution, are designed to yield effervescent draughts, they may be made by first preparing the corresponding granular effervescent salt and compressing this, or the ingredients upon which the effervescence depends may be granulated separately in granules of the same size and then thoroughly dried and mixed just before compression. Thus, if effervescent tablets of lithium citrate or carbonate are wanted, the lithium salt could be granulated with the sodium bicarbonate, while the tartaric acid may be granulated separately with alcohol or water. All effervescent tablets must be carefully protected against moisture in air-tight bottles.

The preparation of compressed tablets in small quantities may be conveniently accomplished at the dispensing-counter, and various combinations readily furnished on extemporaneous prescriptions. The finely powdered ingredients, having been intimately mixed and properly dampened, may be quickly passed through a No. 20 or No. 30 sieve, and the granules rapidly dried by rapidly rotating them on a sheet of smooth paper placed in a sieve or on a perforated tray over a stove or other heated surface; as soon as dry the granules should be weighed and divided into the requisite number of parts, which will then be ready for compression.

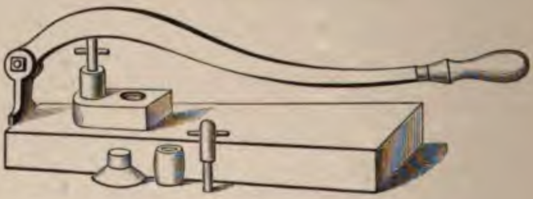
FIG. 248.



Simple mould for compressed tablets.

Different styles of compressors have been designed at various times to suit the purposes of dispensing pharmacists (see Figs. 248 and 249). They are all fed on the same principle, and the mode of operating them differs but slightly. The cylinder, base, and piston are usually made of hardened steel, nickel-plated; the base, which is made to project somewhat into the cylinder, as shown in Fig. 248, having been adjusted, the granular substance is carefully fed into the cylinder from a piece of stiff paper, the piston is inserted over the granules, and compression effected either by a sharp blow from a wooden mallet, or by means of a lever, as shown in Fig. 249. When the tablet has been compressed, it can be removed by lifting the cylinder from the base, the tablet adhering to the concave surface of the piston, and gently tapping the piston with the mallet or lever, which expels the tablet. The Smedley compressor (Fig. 249) is provided with a small receptacle, over which the cylinder and piston can be placed and the tablets discharged directly into it.

FIG. 249.



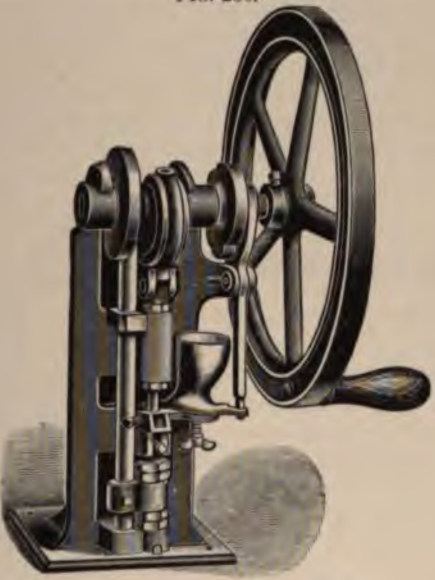
The Smedley compressor.

The greater the pressure applied, the firmer will be the compression, but at the same time the slower will be the disintegration of some compressed tablets; hence only sufficient pressure should be used to cause the particles to cohere properly without crumbling when handled or breaking if allowed to fall.

When too much pressure has been applied some tablets "chip" or "cap," a portion of or the entire upper convex layer showing a tendency to split off. This difficulty may sometimes be remedied by reducing the pressure in the operation, or it may be overcome by adding a little water to the granules, about 1 or 2 drachms to the pound, by means of an atomizer.

If at any time a compressed tablet should become fixed in the cylinder or in the concave depression of the piston, or possibly, if fine powder, having been inadvertently used, some of it should have been forced between the piston and the sides of the cylinder, and thus have fastened the piston, warm water alone should be used to relieve the trouble; never should a sharp instrument be employed to loosen the adhering material, as this would be likely to produce rough surfaces or edges, thereby rendering the compressor unfit for use.

FIG. 250.



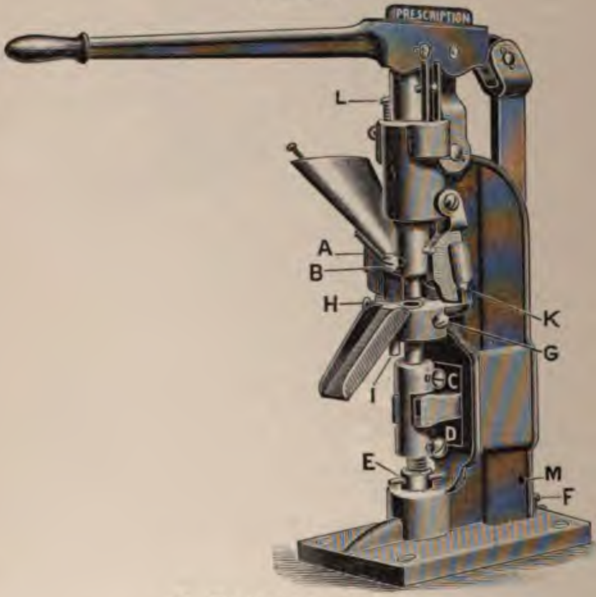
The Eureka tablet machine.

The Eureka tablet machine (Fig. 250) and the Freck tablet compressor (Fig. 251) insure greater uniformity in thickness of the tablets than the apparatus above described. Both machines are provided with an automatic feeding attachment, and hence the tablets can be compressed more rapidly than in other hand machines. In both cases the depth of the mould is regulated by means of a screw, so that after weighing out the material for one tablet and adjusting the mould so it will just hold the same when filled to the top, the tablets are sure to be of uniform weight when compressed.

In the Eureka machine the material is placed in the shoe-shaped hopper shown in the figure, the movement of which is controlled by the large fly-wheel, and which also simultaneously controls the motion of the upper and lower punches. The feeding of the mould is effected from the shoe, which as the wheel is revolved moves forward sidewise with a jerky motion, so that when over the mould the material readily drops into the latter. The further motion of the fly-wheel causes the shoe to return to its original position and at the same time the upper punch descends and compresses the material in the mould, and as the shoe again advances to refill the mould the lower punch rises to push the tablet above the mouth of the mould, whence it is thrown forward into a receptacle by the shoe passing over the mould. The machine is easily understood and readily adjusted, and with a little practice can be made to compress 100 tablets or more a minute.

The Freck tablet compressor, made by the Wm. Freck Co., of Chicago, is apparently one of the best ever made for compressing a small number of tablets at the dispensing-counter or even a hundred or more, inasmuch as the pressure can be regulated, and thus uniformity in thickness and hardness of the tablets be insured. It occupies a space of 5½ by 8 inches, and the lever is of such length

Fig. 251.

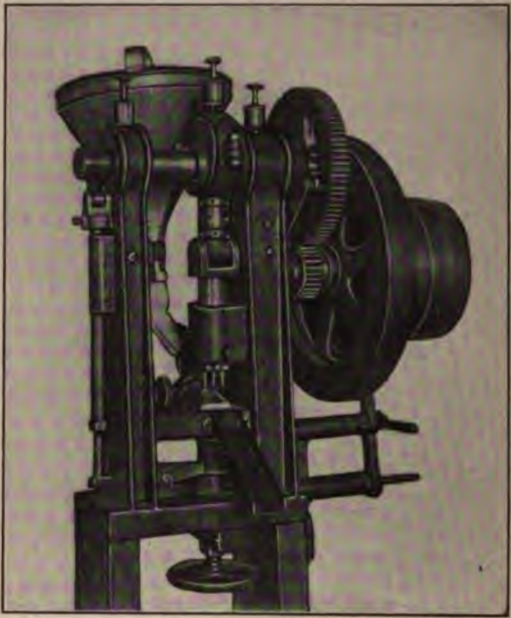


The Freck tablet compressor.

that each pound of pressure upon it is multiplied to 12 pounds on the die. Its construction and mode of operation are best explained by means of the letters shown in the figure: A is the funnel-shaped feeder into which the granulated material is put and which fills the dies; B is a set-screw which holds the upper punch; C is a set-screw which holds the lower punch; D is a set-screw which prevents the regulator from moving; E is the regulator for adjusting the capacity of the dies and consequently the weight of the tablet; F is an adjusting screw for stopping the lower punch even with the surface of the die; G is a set-screw which holds the die; H is a set-screw for the pin I, which swings the feeder; K is the point which holds the feeder to the surface of the machine, and automatically throws the feeder out of the way when the upper punch is descending; L is a screw by means of which the lever-handle may be stopped at a certain distance, so as to give uniform thickness and hardness to the tablets; M is a hole into which a pin is inserted when the handle is raised to its highest point to put it out of gear. As in the Eureka machine, the tablets when compressed are brought above the mouth of the die by the lower punch ascending, and are then removed by the feeder and slide down the chute into a receptacle.

For manufacturing compressed tablets on a large scale, special machinery has been constructed to be operated by steam power. These machines can be so adjusted that a definite quantity of material will be automatically fed into the mould; therefore, as the pressure applied is uniform, the resulting tablets must be of even weight and thickness. Improvements are constantly being made in the various compressors used by large manufacturers, and in Fig. 252 is shown such a tablet machine capable of producing from 75 to 350 tablets per minute, according to the number of dies inserted. Motion is communicated to the machine by means of a belt running over the pulley on the right-hand side, power being carried to the main shaft by means of cog-wheels; this gearing gives the machine great force. The compressing plunger is operated in a vertical direction by means of a cam and an eccentric, a set screw holding the upper punches in the plunger. The machine accommodates from 1 to 5 punches at a time, the punches being readily interchangeable. The lower punches are also held fast by means of a set-screw in a shorter plunger, which in turn is operated in a vertical direction by means of a lever and a bar. The granulated material passes from a funnel-shaped reservoir by means of a flexible tube into a shoe, which moves in a straight line forward and backward, and thus feeds the dies as it passes over them. By means of a corrugated cam, attached to and revolved by a gear, the shoe is given a short shaking motion just as it passes over the dies, causing the material to drop into the latter. When the dies have been filled the shoe recedes and the upper plunger forces down the upper punches into the dies and the material is compressed. The pressure to be exerted on the tablet is regulated by means of a screw and three nuts on the upper part of the upper plunger. After compression the upper punches are withdrawn, the lower punches are caused to rise in the dies by means of a lever, and thus the tablets are brought just above the top of the dies. At this instant the shoe again moves forward and pushes the tablet off the stage, down a chute, into a receiving vessel. The height to which the lower punches may rise must be just flush with the top of the dies, and is regulated by means of a screw in the upright bar on the left of the machine. The amount of material which the dies are capable of receiving depends on the depth to which the lower punches are allowed to drop in the dies, and which is regulated by means of a screw operated by a wheel in the lower part of the machine, beneath the lower plunger.

FIG. 252.



Improved steam-power tablet machine.

In all automatic tablet machines the adjustment of the supply of material to the dies must be made tentatively. The first adjustment is merely approximate, and after the weight of the first tablet thus compressed has been determined, the capacity of the die is increased or decreased, as may be necessary. The proper adjustment having been made, the shoe can supply only as much material as the die will hold, hence the automatic supply must be uniform and exact.

In order to insure a well-shaped tablet, the diameter of the die must be selected in proportion to the weight of each tablet. Thus for material of average density tablets weighing 1 grain may be made with dies $\frac{7}{32}$ of an inch in diameter; 1½ grains will require a ¼ inch die; 2 grains, a $\frac{9}{32}$ inch die; 2½ or 3 grains, a $\frac{5}{16}$ inch die; 3½ or 4 grains, a $\frac{11}{32}$ inch die; 4½ to 5 grains, a ⅜ inch die; 6 or 6½ grains, a $\frac{13}{32}$ inch die; 7 or 8 grains, a $\frac{7}{16}$ inch die; 10 grains, a ½ inch die; 20 grains, a ⅝ inch die, and so on. If the material to be compressed be of high specific gravity, as, for instance, calomel, bismuth subnitrate, etc., a die of smaller diameter must be chosen for the weights mentioned above. Compressed lozenges, which are merely large compressed tablets, with the usual constituents of lozenges, however, are made with ½ to ⅝ inch dies according to the weight of the lozenge. In order to insure good results, the sides of the bore of the die and the concave surfaces and sides of the punches must be kept highly polished. The edges of the punches must be kept sharp and perfect, otherwise there will be an irregularity on the surface of the tablet. After the dies have been used they should be carefully washed and dried and smeared with a little vaselin, to prevent rusting; they should then be stored in a dry place.

TABLET TRITURATES.

This class of preparations was introduced, in 1878, by Dr. R. M. Fuller, of New York, no doubt, with a view of administering small quantities of potent remedies in convenient and readily soluble form. Since then some manufacturing firms have made strong efforts to induce physicians to resort to this method of medication for the purposes of office dispensing. That the growth of homœopathic patronage has largely aided the introduction and use of tablet triturates cannot be denied.

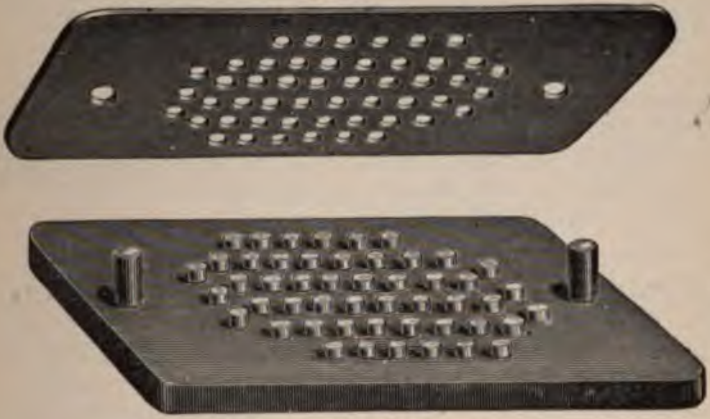
Tablet triturates are made by triturating the active ingredient with either plain sugar of milk or a mixture of sugar of milk and ordinary or cane-sugar (usually in the proportion of 4 or 5 parts of the former to 1 part of the latter), and then forming the mixed powders into a paste with alcohol, alcohol and water, alcohol and syrup, or water alone, which paste is pressed into tablets in appropriate moulds. The composition of the liquid excipient to be employed will vary greatly according to the diluent used, the nature of the medicinal ingredients operated upon, and also the quantity to be present in each tablet, the aim being to produce a partial softness in the mixture which will enable the particles to adhere together in the form of a firm, pasty mass. When simply milk-sugar is used as a diluent, water alone will answer as the excipient in most cases; but when a mixture of milk-sugar and cane-sugar is used, a strongly alcoholic liquid excipient is necessary, on account of the ready solubility of cane-sugar in water, the proportion of alcohol being increased as the quantity of cane-sugar is augmented. For most operations at the dispensing-counter, where no special facilities for rapid drying are at hand, a mixture of 5 parts of milk-sugar and 1 part of cane-sugar, together with an excipient composed of 5 volumes of alcohol and 1 volume of water, will perhaps prove most desirable, as the greater volatility of the alcohol insures more rapid drying of the tablets.

It is essential that the sugar be in very fine powder, in order to yield a smooth paste and perfect tablets; and if the mixture be passed through a No. 120 sieve before making the paste, the results will be all the better. A few cases will occur in which sugar and other organic matter are inadmissible as a diluent, owing to chemical changes likely to occur; as, for instance, potassium permanganate, silver nitrate, etc.; finely powdered kaolin, or pipe-clay, should then be used with water as an excipient.

Tinctures and fluid extracts, unless strongly alcoholic, are made into tablet triturates with more or less difficulty, according to the amount of fluid to be represented in each tablet, and may require evaporation to dryness with a portion of the sugar, so as to be subsequently reduced to fine powder, prior to converting into a suitable paste. The presence of glycerin, especially if in large proportion, is objectionable, since it keeps the extractive matter soft and prevents proper drying of the tablets. In some instances it will suffice to concentrate the fluid by evaporation and use it, in place of an excipient, for moistening the mixed powders; but this plan can only be followed when the proportion of fluid ordered is small or when it has been made with a strongly alcoholic menstruum. Solid extracts can be introduced only in small proportions, and may then be incorporated as indicated under Compressed Tablets; more than one-fourth or one-third of the total weight of the tablet triturate is not advisable. In such cases, and also in the case of tablets to contain various amounts of tinctures or fluid extracts made with hydro-alcoholic menstrua, a mixture of milk-sugar and starch in varying proportions will be found the best diluent. Such masses are often difficult to form into smooth tablets, and the tablets when dried are often very hard. Tablet triturates containing $\frac{1}{4}$ grain or more of solid extract or 1 minim or more of hydro-alcoholic fluid extract can be made more friable by using a mixture of milk-sugar and starch as diluent and granulating the well-mixed mass as directed under Compressed Tablets, and subsequently compressing the dry granules by means of a compressing apparatus into shape similar to that of tablet triturates. Enough diluent should be used to make the finished tablet weigh about $1\frac{1}{2}$ grains each. The pressure is readily regulated so as to produce a friable tablet. The punches used for this purpose should have flat surfaces, to insure the customary shape and appearance of tablet triturates, although concave punches will yield tablets equally friable. Substances of a volatile or deliquescent character, or such as are readily oxidized upon exposure to air, are wholly unfit for tablet triturates; hence camphor, creosote, calcium sulphide, arsenic iodide and bromide, potassium citrate, scale salts of iron, phosphorus, and the like, should never be dispensed in this form.

Automatic machines for making tablet triturates have not yet been constructed, and the apparatus generally used, whether for small quantities at the dispensing-counter or in the manufacture of tens of thousands in the laboratory, consists of two plates, as shown in Fig. 253. The plates, although sometimes constructed of metal, are preferably made of hard rubber, the upper one being perforated and the lower provided with a corresponding number of pegs, which fit accurately into the perforations of the upper plate. In order to insure the exact position of the pegs when the upper plate is brought down over them, two guide-pins are fastened to the lower plate, one near each side; these extend above the pegs and enter two corresponding holes in the upper plate. As a rule, the plate moulds are made to prepare 50 or 100 tablet triturates at one time, although some are provided with 200 or more perforations, and a few with only 25. The perforations in plates of the standard size adopted for tablet triturates measure $\frac{7}{32}$ of an inch in diameter, and $\frac{1}{8}$ of an inch in depth. In a few instances moulds are used with perforations $\frac{9}{32}$ of an inch in diameter and $\frac{1}{8}$ of an inch in depth; larger tablets are now generally made by compression, since the same weight of material can by this method usually be obtained in smaller bulk.

Fig. 253.

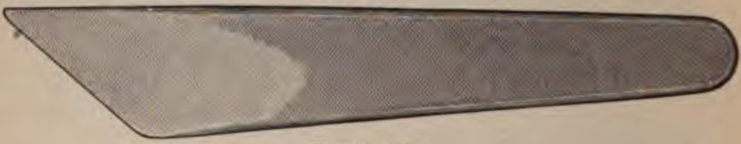


Hard-rubber mould for tablet triturates.

Hard-rubber moulds require considerable care in cleaning and in storing them when not in use, in order to preserve the original perfect shape. They should never be exposed to heat, either by using hot water for washing or dry heat for drying them, as the moulds are thereby warped and the accurate adjustment of the pegs and perforations is destroyed; when thus warped, the moulds can only be used with great difficulty, and soon become worthless. A narrow, stiff paint-brush will be found very serviceable in cleaning the moulds, and water at the ordinary temperature should be used for washing the plates; sometimes alcohol, or even acids, may be necessary to remove material tenaciously adhering to the moulds, but never should a sharp instrument be used in the perforations or on the pegs, as the smooth surfaces are likely to be scratched thereby. After the plates have been carefully cleansed and rinsed with cold water they should be dried with a soft towel, the water remaining between the pegs being readily shaken out; when dry, the perforated plate should be placed in proper position on the peg-plate, and the whole laid aside on a level, solid surface, away from heat.

When a suitable paste has been made the perforated plate is placed upon a level surface, preferably a thick glass plate, and, by means of a horn spatula of the shape shown in Fig. 254, the mass is forced into the holes so as to fill these completely, any excess of material being removed with the spatula; the plate is then reversed and, if necessary, more of the mass is forced into the holes until they are completely filled and both sides present a smooth, solid surface. The operation is best explained as follows: The operator grasps the spatula in such a manner that the forefinger rests on the flat surface near the acute angle of the diagonal edge, with the middle finger resting near the obtuse angle of the same edge; the thumb rests against the long side, and the third and little fingers against and slightly around the short side of the spatula. The mass having been placed on the mould under the spatula, the latter is drawn with pressure over the mould diagonally toward the operator. After the required number of holes have been filled, the upper plate is carefully brought down over the lower one with the marks or numbers at the end of the two corresponding, and by the aid of the guide-pins the pegs are pressed into the corresponding holes and the tablets thus forced out, remaining on the ends of the pegs; after a few moments they may be removed, either by inclining and tapping the plate or by carefully brushing them into a suitable receptacle, preferably a bolting-cloth sieve. The tablets should then be dried either by exposure to the ordinary room-temperature, protecting them from dust, in closets supplied with circulating warm air, or in small quantities on a perforated tray near a stove or register, as the nature of the medicinal ingredients may permit. By means of hard-rubber moulds holding 100 tablets each, experienced operators average from 6000 to 8000 tablet triturates per hour, unless the material be especially difficult to manipulate.

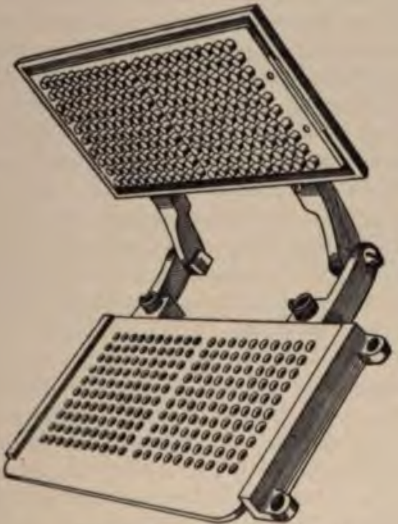
FIG. 254.



Horn spatula.

Some manufacturers use an apparatus somewhat differently constructed, as shown in Fig. 255. The two plates are held in frames hinged together and so arranged that the peg-plate can be brought down accurately over the perforated plate carrying the tablets, and by pressing the pegs down through the perforations the tablets are made to drop out upon a sheet of paper placed underneath for their reception. The weight of different kinds of tablet triturates made with moulds of the standard size mentioned above will vary considerably according to the density of the mass being manipulated. Thus tablets containing $\frac{1}{4}$ grain of morphine sulphate each, will weigh about 1.2 grains; tablets containing $\frac{1}{4}$ grain of calomel will weigh about 1.4 grains; and tablets containing 1 grain of calomel will weigh from 1.9 to 2 grains each; while the size of all these tablets will be the same. The weight of the tablets will also be considerably influenced by the pressure upon the spatula exerted by each individual operator during the process of moulding, which varies with nearly every person, and hence in large manufacturing establishments operators are kept at work on certain lines of tablet triturates with which they have become familiar so as to insure uniformity in weight. The weight of a certain tablet having been ascertained, a memorandum should be made of the details regarding combination, diluent, and excipient, for future reference.

FIG. 255.



Colton's tablet triturate mould.

Every formula for new tablet triturates must be determined tentatively in order to ascertain the exact amount of sugar of milk or other diluent required. The simplest plan is to weigh off enough of the active ingredients to make a given number of tablets (say 25 or 50); mix this with a quantity of diluent known to be insufficient, moisten with the necessary excipient, and press the mass into the holes of the plate intended to be used. Then moisten more of the same diluent with the excipient, and with this paste fill the holes remaining unfilled from the first operation; smooth off both sides of the tablets, place on the ejecting-pegs and force the tablets out. For larger operations the tablets should then be thoroughly dried and weighed, the weight of the dry tablets less the weight of active ingredients used representing the weight of the diluent required to make the given number of tablets. In small operations, particularly those of the dispensing-counter, the drying may be omitted, and, instead, an extra number of tablets (4 or 5) made out of the plain diluent, added to the number first obtained, before the whole is thoroughly mixed in a mortar; this extra material is necessary because the first tablets, when worked up again in the mortar, generally form a more compact mass, and hence would prove insufficient for refilling the required number of perforations. The porous nature of most tablet triturates and the very fine state of division of the ingredients render it essential that the tablets be carefully kept in dry, tightly stoppered amber-colored vials, which protect them perfectly against the air, moisture, and the effects of the light. They should be stored in a cool and dry place. Small amber-colored homœopathic vials are likewise the best receptacles for dispensing these tablets. Tablet triturates containing substances readily affected by air or light are often made into compressed lenticular-shaped disks and subsequently coated with sugar or chocolate.

Hypodermic tablets are simply tablet triturates intended for the convenient preparation of solutions for subcutaneous injection. Since they contain definite quantities of the active agents, they are admirably adapted for physicians' use at the bedside, and are very extensively employed. As a rule, pure sugar of milk or pure cane-sugar is used as the vehicle, although sodium sulphate has also been employed by some manufacturers. They are made in the hard-rubber moulds already described, the perforations being usually $\frac{5}{32}$ inch in diameter and $\frac{1}{16}$ or $\frac{1}{8}$ inch in depth. This produces a tablet that can readily be dropped into the barrel of a hypodermic syringe, in which it is quickly dissolved upon addition of 10 or 15 minims of water and subsequent agitation.

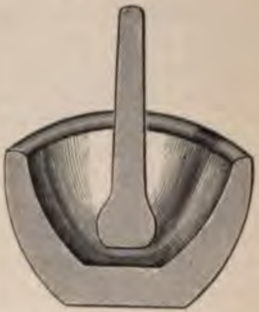
Tablet saturates differ from tablet triturates only in the manner of introducing the medicinal agents. They are made by first preparing plain sugar-of-milk tablets, in the moulds already described, and having placed the tablets, when dry, on a glass plate, the desired quantity of tincture, fluid extract, or solution, is dropped upon each tablet individually from a pipette. A glass cover is then placed over the tablets and the fluid allowed to saturate them uniformly, after which they are dried in a current of warm air.

CHAPTER XXXI.

POWDERS.

In addition to what has already been said about pulverization, in the chapter of Mechanical Subdivision of Drugs, there remains yet to be considered the administration of medicines in powder form, which, presenting certain advantages, is still largely employed by physicians. The powder form is a most convenient method of giving medicines in the case of very young children and persons who are unable to swallow pills, as well as where the fluid form is unavailable for any reason. It is true, many substances are not suited for administration in powder form, particularly bulky vegetable powders, deliquescent salts, and such as contain large quantities of water of crystallization, as sodium phosphate or sulphate, etc.; but while the fluid form of medicine is probably to be preferred in the majority of cases, the bitter or nauseous taste of some substances becomes more marked in solution than in the dry state. Among the substances best adapted for dispensing in powder form are insoluble chemicals, such as calomel, bismuth salts, mercury with chalk, some salts of the alkaloids, and vegetable drugs given in small doses, such as ipecac, opium, and catechu. Physicians frequently direct their patients to dissolve or mix the powder in water, and in such cases the powder form is preferred on account of convenience or for reasons of economy.

Fig. 256.



Porcelain powder-mortar (sectional view).

Powders, as a rule, are composed of two or more substances; to insure an intimate and uniform mixture they must be triturated in a mortar, preferably made of porcelain, of the shape shown in Fig. 256, this style presenting a sufficient broad surface at the base, whilst its curved sides prevent the ejection of material during trituration. It is assumed that in the majority of cases the individual ingredients are already in the state of very fine powder, and therefore only require thorough mixing, which is best accomplished by trituration with light pressure only, so as to avoid caking and sticking to the sides of the mortar; the contents of the vessel should also occasionally be scraped from the pestle and sides of the mortar if necessary, as this aids more perfect admixture. Whenever substances which are themselves in a coarsely powdered or granular condition are ordered in a powdered mixture, they must be reduced to a very fine powder by themselves, no attempt being made to reduce them in the mixture.

A few general rules will serve for guidance in the preparation of mixed powders. Whenever sugar is one of the ingredients it should be of the kind known as bolted or lozenge sugar. When small quantities of potent or other substances are to be dispensed in powders, they should first be well triturated with a portion of the diluent, and finally incorporated with the remainder of the more bulky powders; or, if no diluent has been ordered, they should be triturated with a small quantity of sugar of milk, to insure their more uniform distribution in the mixture. The proper plan is to place about 5 grains of sugar of milk in the mortar, add the active ingredient, and then triturate thoroughly, as, by this means, more accurate subdivision is effected, and none of the active material is likely to adhere to the sides of the mortar. Soft extracts and essential oils must be treated in the same manner.

Whenever physicians prescribe quantities which cannot be weighed conveniently, such as $\frac{1}{6}$, $\frac{1}{10}$, $\frac{1}{24}$, or $\frac{1}{32}$ of a grain, and metric weights less than 10 milligrammes, the plan of preparing a dilution of the substance with sugar of milk, by trituration, in such proportions that a weighable amount of the mixture shall represent the desired quantity of active ingredient, as indicated on page 341, should invariably be followed, as by this method accuracy of division is best obtained.

Certain substances of a crystalline structure—notably also those of a resinous character—have a tendency to become electrical by friction, particularly if pressure be employed; such bodies are said to be idioelectric, and must be triturated lightly, or, if pressure is necessary to reduce them to fine powder, they must be sprinkled with a little alcohol, whereby the trouble is obviated, or the powder, which adheres firmly to the mortar and pestle, and is prone to fly off in all directions if scraped with a spatula, must be set aside for a while until the electric condition has disappeared. To this class belong common pine resin, and the resins of guaiacum, jalap, and scammony, also quinine alkaloid, acetanilide, salol, phenacetin, and others. The removal of these in fine powder form from the mortar is attended with more or less difficulty unless previously slightly dampened.

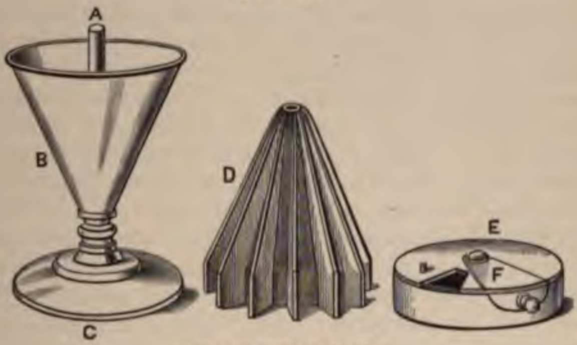
When substances which differ materially in specific gravity are to be mixed in powder form—as, for instance, bismuth subnitrate with magnesia, sodium bicarbonate with charcoal, or zinc oxide with lycopodium—the best plan is to place the heavy substance in the mortar and incorporate the lighter body gradually by adding small portions at a time. Calcined magnesia and charcoal are also more readily mixed if the charcoal be gradually added to the magnesia with very light trituration; only in this manner can a powder of uniform appearance be obtained. Whenever large quantities of these powders are to be mixed, perfect blending may be achieved by shaking them together in a bottle for some time, and then passing the mixture repeatedly through a bolting-cloth sieve.

Since some substances when triturated together cause chemical decomposition, attended in a few cases also with explosion, considerable care must be observed in mixing them; the offending ingredient should be reduced to fine powder by itself, and then cautiously mixed on paper with the other powders. Such conditions arise when potassium chlorate or permanganate is to be mixed with organic substances, as sugar, starch, tannin, gum-arabic, and also sulphur and sulphides, or when lead acetate and zinc sulphate or borax and alum are triturated together.

Powders, whether simple or compound, intended for external application, by dusting or insufflation, must be passed through a fine bolting-cloth sieve, and should not then be triturated again before they are dispensed.

In the majority of cases medicines prescribed in powder form are dispensed in divided doses; although absolutely accurate division can only be obtained by weighing, this plan is rarely followed since practice will soon enable one to omit this tedious method. Usually the operator divides the mixed powder by the eye, either directly on the powder papers or by shaping the powder into a rectangle on a graduated tile, and dividing this into the requisite number of parts; an experienced dispenser is able to make quite accurate divisions from the mortar direct to the paper.

FIG. 257.



Michael's powder-divider.

To facilitate the division of doses at the dispensing-counter a very neat powder-divider was designed, some years ago, by J. C. Michael, a former pharmacist; it is shown in Fig. 257. The apparatus consists of a cup with base attached, a set of three dividers, with 8, 10, and 12 wings respectively (one of which is shown in the illustration), and a cap with sliding door. It is operated as follows: The thoroughly mixed powder is placed in the metallic cup, B, and, after shaking down so as to obtain a level surface, the metallic divider D is slipped over the rod A, and allowed to work its way slowly down to the bottom of the cup; by slight manipulation, such as gently rotating the divider, the powder will be divided into as many equal parts as wings are attached to the divider. The cap E, which fits snugly over the projecting wings of the dividers, and is held in position by means of a central pin, is next attached, and, the cup having been inverted, the rod A is removed by turning the base C held by a bayonet-joint, and withdrawing the rod from the centre of the divider. The powder will now be found transferred to the cap, but divided, as before, since the wings of the divider extend beyond the rim of the cup to the full depth of the cap; by bringing the apparatus over the centre of the paper one portion can be deposited at a time by pulling back the slide F, and allowing the powder to fall upon the paper. It is, of course, important, when placing the cap on the cup, so to adjust it that the edges of the opening be on a line with two of the wings, which is best done with the slide open. By carrying the apparatus from paper to paper and rotating the divider, each succeeding section can be emptied and thus rapid division of the mixture be effected. The whole apparatus is nickel-plated, which protects it against rust. Very accurate work can be done with this apparatus, and the necessary experience for rapid manipulation is easily acquired.

Another convenient device for those who do not wish to entrust division of powders to the eye is the Diamond powder-divider. This consists of a nickel-plated shallow metal trough, closed at one end and graduated on both sides; the powder having been introduced, a hard-rubber plug is inserted at the open end and pushed up to the graduation indicating the number of divisions to be made. After levelling the surface of the powder by means of an accompanying flat bar, with handle attached exactly fitting into the trough, the rubber plug is removed and a quantity of the material, equivalent to one dose, as indicated by the divisions of the graduated sides, is transferred to paper by the aid of a spatula of the same width as the interior of the trough. The dimensions of the trough are 9 inches in length, 1 inch in width, and $\frac{3}{8}$ of an inch in depth.

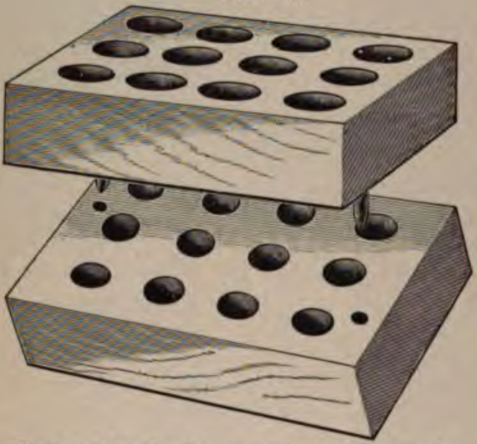
For enclosing the divided doses of powder, either well-calendered or parchment paper may be used; the latter is now preferred by many pharmacists, as it offers a protection against the moisture of the air. Even those who use glazed white paper will find either parchment or waxed paper necessary for volatile or hygroscopic substances. Powder-papers should be folded uniformly, hence it will be found advantageous to keep in stock a supply of the various sizes, already creased. This is readily done by folding the paper over a piece of stiff metal of suitable size, with rounded edges to prevent cutting, in such a manner that a narrow margin, about $\frac{1}{8}$ inch wide, is made on one of the long sides; the straight edge having been brought up against the crease of the margin, both ends are folded back to about the centre of the piece of metal and firmly pressed down with a horn spatula. The two sides are now folded over the edges of the metal plate and also firmly pressed, after which the creases are all opened and the plate is removed. Such creased powder-papers not only insure absolute uniformity in size and shape, but have also been found very convenient in economizing time at the prescription-counter. Some pharmacists prefer to fold each paper containing the powder over a powder-box or specially constructed adjustable powder-folder. The habit of flattening the powder within the paper by pressing it with a spatula is a bad one, and should never be followed, as it is likely to cause the powder to cake, and often interferes with its proper administration in liquids. To prevent any of the material from leaving the paper, one of sufficiently large size should be used, that the creases where the sides have been folded over may be pressed down with a spatula; this effectually prevents leakage.

A small number of powders in papers (two or three) are usually dispensed in an envelope, while the regular oblong powder-boxes are used for larger numbers. When not divided into doses the powder is dispensed either in round paper boxes (never in paper, unless intended for use at one time) or in wide-mouth bottles; the latter method is necessary if the ingredients attract moisture or if very volatile substances are present, and will also be found convenient when travelling. When bottles are used, a piece of glazed paper should be inserted between the neck of the bottle and the cork, to prevent particles of the latter from falling into the powder.

While, as a rule, medicines in powder form are administered to the patient either dry on the tongue, or in solution, or admixed with a small quantity of water, physicians frequently direct them to be enclosed in capsules or wafers, with the view to disguise the taste. The filling of definite quantities of a powder into capsules is rather troublesome, on account of the small orifice of the latter; and to facilitate the operation recourse is had to a device especially designed for that purpose. Small blocks of hard wood are provided with 12 or 24 sockets of such depth that the capsules, when placed therein, shall project about one-third above the edge; another piece of wood, with perforations corresponding to the sockets, is placed over the lower block, after the capsules have been inserted, and then, by means of a suitable funnel (of hard rubber or metal), the powder is transferred to the capsules and somewhat compressed with a plunger exactly fitting the throat of the funnel and the capsule. After all the capsules have been filled the upper perforated block is removed and the cover slipped over the projecting ends of each capsule. For the various sizes of capsules different blocks and funnels are required. In Figs. 258 and 259 are shown the blocks and a suitable funnel; the latter has a wide rim flattened on one side and a short tube, whereby the powder is more conveniently fed into the capsules.

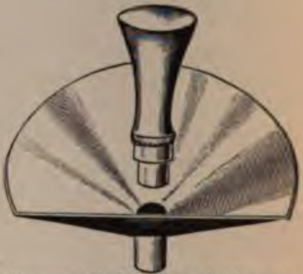
To facilitate the filling of simple and compound powders into gelatin capsules, an apparatus known as Ihrig's capsule-filler was devised in 1899, for which it is claimed that the filling can be done more expeditiously than by any other method and with remarkable accuracy as to weight. As shown in Fig. 260, the apparatus consists of a stationary metal base with a square polished movable plate or table having perforations for holding the various sizes of capsules, and which can be raised or lowered by means of a thumbscrew. The perforations are arranged in fields of 60 for each Nos. 2, 3, 4, 5, and 00 gelatin capsules, and of 56 for each Nos. 1 and 0. When in position for filling, the lower portion of the capsules should rest on the base and the upper plate be raised so that the top of the capsules is slightly below the surface of the upper plate. A metal square accompanying each apparatus is next placed in proper position, as shown in the illustration, so as to separate the capsules to be filled from perforations not in use, and the powder having been distributed with a spatula or camel-hair pencil, is pressed into the capsules by means of a metallic triple punch, as shown in Fig. 261. In order to enable the operator to put the tops on the capsules, the upper plate is lowered, as shown in Fig. 262, when the cap can be quickly adjusted. An important point in filling powders into gelatin capsules is to use capsules of the

Fig. 258.



Hard-wood blocks for supporting empty capsules while being filled.

Fig. 259.



Davenport's funnel and plunger for filling capsules.

Fig. 260.

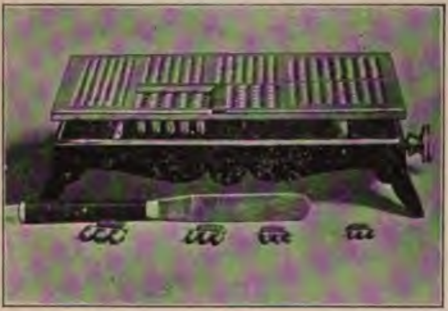


FIG. 261.

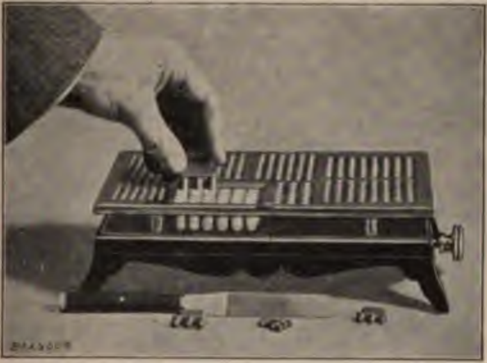
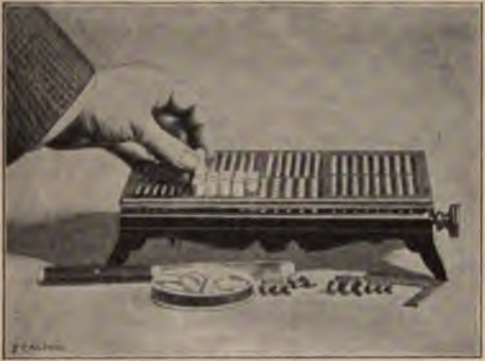


FIG. 262.

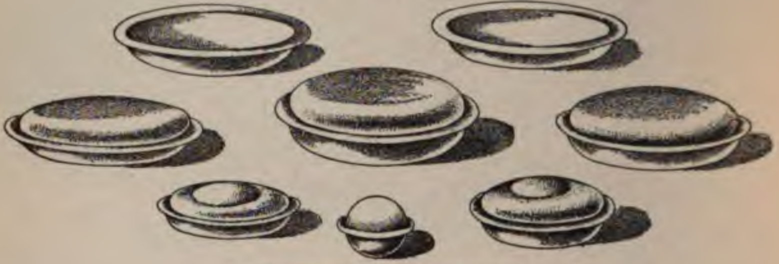


proper size to hold the required quantity of powder nicely, and this must be determined tentatively. Manufacturers of gelatin capsules suggest the following guide for approximate capacity of empty capsules, which will enable pharmacists to make a suitable selection without much trouble, bearing in mind, however, that the capacity varies according to the degree of compression exerted in filling:

Size of Capsule.	No.	00.	0.	1.	2.	3.	4.	5.
Bismuth Subnitrate	Grs.	20	14	10	8	6	4	2
Cinchonidine Sulphate	Grs.	8	6	4	3	2	1½	¾
Dover's Powder	Grs.	12	8	6	4	3	2	1
Powdered Aloes	Grs.	10	7	5	4	3	2	1
Powdered Rhubarb	Grs.	12	8	6	4	3	2	1
Quinine Sulphate	Grs.	8	6	4	3	2	1½	¾
Salicin	Grs.	10	7	5	4	3	2	1
Salicylic Acid	Grs.	8	6	4	3	2	1½	¾

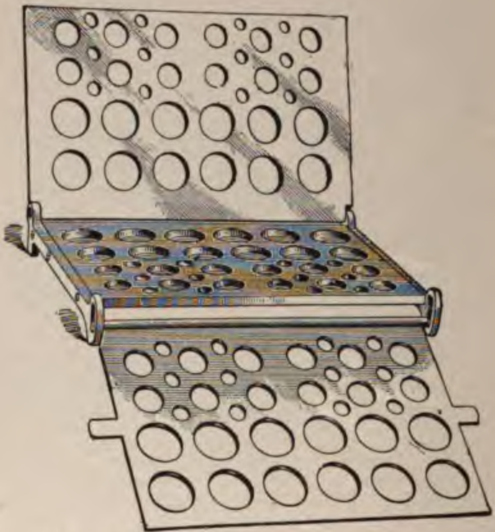
The use of wafers is not so much in vogue in this country as in Europe, but they are, in many respects, preferable to capsules; less compression of the material is necessary, and the envelope, made of rice-flour, is more readily disintegrated in the stomach. Sometimes small square or circular sheets of wafer paper are ordered, and the patient is directed to enclose each dose as wanted; this is done by dipping the wafer into cold water, whereby it is rendered flaccid; it is then laid over a spoon, the powder placed in the centre, and, the edges having been folded over, it is swallowed with a draught of water.

FIG. 263.



"Konseals" or rice-flour cachets.

FIG. 264.



The "Konseal" filling and closing apparatus.

The small round wafers known as cachets are intended to be filled and sealed by pharmacists. Various appliances have been proposed, of which that extensively used in Europe in connection with Mohrstadt's cachets is decidedly the most desirable, as it is simple in construction and quickly operated; the device is sold in this country by J. M. Grosvenor & Co., of Boston, as the "Konseal" filling and closing apparatus, and is fully illustrated and described further on. The use of the word "konseal" in place of cachets or wafers does not strike one as particularly appropriate, and is to be regretted. The "konseals," or cachets, are concave disks made of rice-flour and water; they are of convenient form, perfectly digestible, keep permanently for years, and are prepared in six sizes, shown in Fig. 263, varying in capacity from 1 to 10 or 20 grains of dry powder.

Fig. 265.

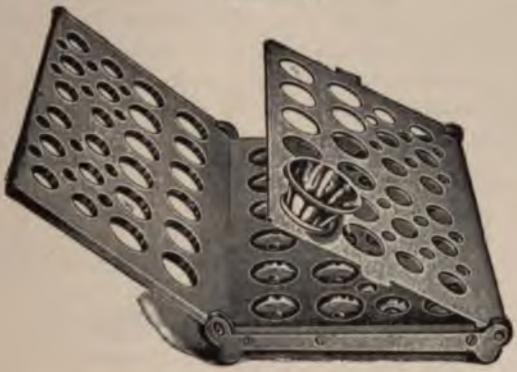
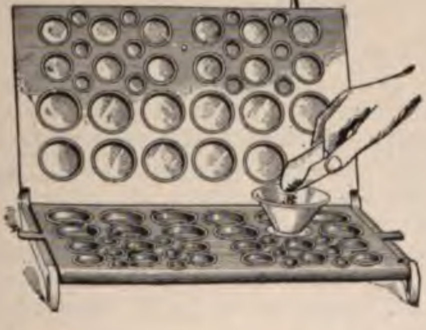
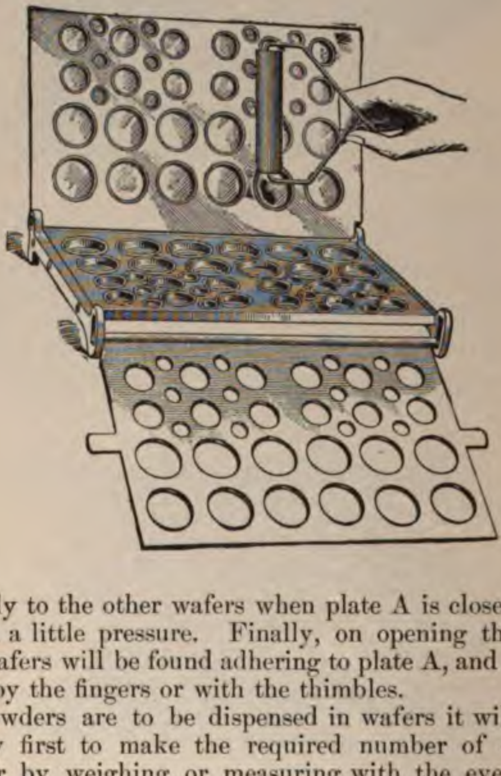


Fig. 266.



The "Konseal" filling and closing apparatus consists of three nickelled plates suitably hinged (see Fig. 264); the centre plate B is provided with 36 concave depressions, to suit the different sizes of wafers, and the two other plates (A and C) are perforated in a manner to correspond exactly to the depressions in B. The wafers are first pressed into the spaces of A and B adapted for the particular size selected; one of the short funnels accompanying the apparatus having been inserted into the proper perforation of plate C, the latter is folded over on to plate B, as shown in Fig. 265. The powders are next poured into the wafers, as shown in Fig. 266, and, if necessary, owing to large bulk, are slightly compressed with the thimble furnished for the purpose; small quantities of the powder can be conveniently fed into the wafers without the use of funnel or thimble. When the required number of wafers has been filled plate C is turned back from plate B, and the damping roller (not too wet) passed over the wafers in plate A, as shown in Fig. 267, whereby the edges of the wafers are sufficiently moistened to cause them to adhere closely to the other wafers when plate A is closed down over plate B with a little pressure. Finally, on opening the apparatus, the sealed wafers will be found adhering to plate A, and can be easily pushed out by the fingers or with the thimbles.

FIG. 267.



When powders are to be dispensed in wafers it will, of course, be necessary first to make the required number of divisions on paper, either by weighing or measuring with the eye; in Europe a graduated glass tube with hard-rubber piston is said to be used for the same purpose.

The Pharmacopœia furnishes formulas for the preparation of 9 compound powders, but directs the division into doses in only 1 case. The following is a list of the official powders and their composition:

COMPOUND POWDERS OF THE U. S. PHARMACOPŒIA.

Latin Name.	English Name.	Composition.	
Pulvis Acetanilidi Compositus	Compound Acetanilide Powder	Acetanilide	70 Gm.
		Caffeine	10 "
		Sodium Bicarbonate	20 "
Pulvis Aromaticus	Aromatic Powder	Saigon Cinnamon	35 Gm.
		Ginger	35 "
		Cardamom (deprived of capsules)	15 "
		Nutmeg	15 "
Pulvis Cretæ Compositus	Compound Chalk Powder	Prepared Chalk	30 Gm.
		Acacia	20 "
		Sugar	50 "
Pulvis Effervescens Compositus	Compound Effervescing Powder (Seidlitz Powder.)	Sodium Bicarbonate	2.583 + Gm.
		Potassium and Sodium Tartrate	7.749 + "
		Tartaric Acid	2.250 "
Pulvis Glycyrrhizæ Compositus	Compound Powder of Licorice	Senna	180 Gm.
		Glycyrrhiza	236 "
		Washed Sulphur	80 "
		Oil of Fennel	4 "
		Sugar	500 "
Pulvis Ipecacuanhæ et Opii	Powder of Ipecac and Opium (Dover's Powder.)	Ipecac	10 Gm.
		Opium	10 "
		Sugar of Milk	80 "
Pulvis Jalapæ Compositus (Pulvis Purgans.)	Compound Powder of Jalap	Jalap	35 Gm.
		Potassium Bitartrate	65 "
Pulvis Morphinæ Compositus	Compound Powder of Morphine (Tully's Powder.)	Morphine Sulphate	1.5 Gm.
		Camphor	32 "
		Glycyrrhiza	33 "
		Precipitated Calcium Carbonate	33.5 "
Pulvis Rhei Compositus	Compound Powder of Rhubarb	Rhubarb	25 Gm.
		Magnesia	65 "
		Ginger	10 "

SPECIAL REMARKS.

In the case of compound chalk powder and compound jalap powder, the ingredients being already in a state of fine powder, simple admixture with light trituration is necessary.

Pulvis Aromaticus; Aromatic Powder.—Cardamom deprived of the capsules is directed, because the latter are inert and cannot be reduced to fine powder; the crushed seed and coarsely powdered nutmeg (best obtained by grating) can readily be brought to a state of fine powder by trituration with about one-half of the cinnamon, using at the same time slight pressure.

Pulvis Effervescens Compositus; Seidlitz Powder.—The so-called "Seidlitz Mixture" of commerce is not always of the composition prescribed by the Pharmacopœia; hence it is better to make it, as wanted, by mixing 1 part of sodium bicarbonate with 3 parts of Rochelle Salt. The alkaline mixture is usually put up in blue papers and the acid powder in white paper. The small wooden measures intended for rapid division of the powders are, as a rule, not uniform; moreover, the quantity of material that can be compressed into these measures varies considerably with the condition of the atmosphere, which renders them unreliable; hence the prescribed quantities should be weighed for each paper, being 10.333 + Gm. (160 grains) of Seidlitz Mixture and 2.25 Gm. (35 grains) of tartaric acid. The powders should be protected against dampness, and it will be found advantageous to dispense the acid in parchment paper.

Pulvis Glycyrrhizæ Compositus; Compound Licorice Powder.—By triturating the oil of fennel with a part of the sugar, before adding the other ingredients, its distribution in the powder is greatly facilitated. The use of oil in place of powdered fennel is advantageous, as the finished mixture can then readily be passed through a No. 80 sieve, and the finer the powder the better it is; moreover, the product will not assume by age that disagreeable odor which has been observed when the powdered seed is used.

Pulvis Ipecacuanhæ et Opii; Powder of Ipecac and Opium, or Dover's Powder.—The Pharmacopœia directs sugar of milk to be used in rather coarse powder, so that the fragments of crystals, being very hard, may serve to grind the vegetable powders to an impalpable condition during the necessary prolonged trituration. Since the finished product contains 10 per cent. each of ipecac and opium, an average adult dose, .0648 Gm. (10 grains), of the powder will represent 0.0648 Gm. (1 grain) of each active ingredient. Dover's powder is a favorite diaphoretic.

Pulvis Morphinæ Compositus; Compound Morphine Powder, or Tully's Powder.—The value of Tully's powder resides in the camphor and morphine present, the licorice and precipitated chalk serving simply as diluents. In order to secure the camphor in very fine division, it must be triturated with a little alcohol and at once mixed with the diluents, the morphine being incorporated by adding to it the other mixed powders in small quantities at a time. Each gramme of the finished product represents 0.015 Gm. of morphine and 0.32 Gm. of camphor, or 10 grains contain nearly $\frac{1}{6}$ grain of the former and about 3 grains of the latter. Owing to the volatile nature of the camphor, the powder should always be dispensed in paraffin or parchment paper.

Pulvis Rhei Compositus; Compound Rhubarb Powder.—The best plan for thoroughly blending the magnesia with the rhubarb and ginger will be to mix the last-named two powders first, then add the magnesia, in small quantities at a time, triturating without pressure, and, finally, pass the whole mixture through a bolting-cloth sieve.

TRITURATIONS.

Under this head the Pharmacopœia recognizes mixtures of remedial agents and sugar of milk, in the form of a very fine powder, made in such proportions that each Gm. of the mixture shall contain 0.100 Gm. of the active ingredient, or 1 grain represent $\frac{1}{10}$

of a grain. The general official directions for making triturations are to mix the substance in a mortar with an equal weight of sugar of milk, both in moderately fine powder, and then to triturate thoroughly together, adding fresh portions of sugar of milk from time to time, until 9 parts of the latter shall have been mixed with 1 part of the substance, and the whole reduced to a very fine powder. The advantage of using moderately fine powder in the beginning consists in the more intimate admixture of the ingredients brought about by the prolonged trituration necessary for reduction to fine powder.

But one trituration is officially designated, namely, "Trituration of Elaterin"; this is a mixture of 10 Gm. of elaterin and 90 Gm. of sugar of milk, made according to the general directions given above.

OIL-SUGARS.

Powders of this class are chiefly used as correctives or flavoring agents, and are prescribed by physicians under the name Oleosaccharа or Elæosacchara. These are extensively employed in Europe, particularly in Germany, but are not recognized in our Pharmacopœia.

Oil-sugars are composed of powdered cane-sugar and volatile oil only, each drachm of the former requiring the addition of 2 drops of the latter, the two being thoroughly mixed by trituration; they should be freshly made when wanted. When prescribed, the particular kind is designated by specifying the name of the oil to be used; thus, oleosaccharum or elæosaccharum anisi, menthæ piperitæ, fœniculi, limonis, etc., meaning oil-sugar of anise, peppermint, fennel, lemon, etc.

CHAPTER XXXII.

GRANULAR EFFERVESCENT SALTS.

THE administration of remedial agents in the form of effervescent draughts has become quite popular during the past twenty years, and, as the solutions are only agreeable when freshly made, it is necessary to have the remedies in convenient form for extemporaneous preparation of the draught. Such a form is presented by the granular effervescent salts of the market. While the Pharmacopœia recognizes but 5 preparations of this class, a very large number is offered by manufacturers, and, as they are easily made, without elaborate apparatus and appliances, their preparation is within the reach of all pharmacists. The combination consists of the active medicinal ingredients, the effervescent agents, and frequently sugar, to improve the taste. As a base for producing the effervescent draught, sodium bicarbonate, with citric or tartaric acid, or a mixture of the two acids, is employed. Effervescent granules made with citric acid are preferable to those made with tartaric acid, and will keep better, since they are much firmer; as a rule, a mixture of the two acids is used. All ingredients must be dry and mixed in the form of fine powder. The method of granulating the mixture will vary with different operators; while for small quantities, such as the pharmacist is likely to handle, dampening of the powders with 95 per cent. alcohol and then rubbing the paste through a sieve offers the most convenient plan, large manufacturers subject the mixed powders to a temperature sufficiently high to fuse some of the constituents, and thus obtain the necessary adhesiveness.

The Pharmacopœial directions for the preparation of granular effervescent salts are to place the mixed powders on a plate of glass or in a dish, in an oven heated to between 93° and 104° C. (199.4° and 219.2° F.). When the mixture, by the aid of careful manipulation with a wooden spatula, has acquired a moist consistence, it is to be rubbed through a No. 6 tinned iron sieve, the resulting granules being dried at a temperature not exceeding 54° C. (129.2° F.). In order to prevent drying out of the powder before it undergoes semifusion, the plate or dish should be heated in the oven some time before the powder is to be heated.

Whenever sugar is present in the mixture to be granulated, care must be observed in the application of heat, to avoid a yellowish coloration of the granules; moreover, the sodium bicarbonate is likely to lose carbon dioxide if heated beyond 72° C. (161.6° F.), thus rendering the preparation deficient in effervescent properties. If alcohol be used to make a pasty mass of the well-mixed powders, these difficulties are avoided, since a temperature not above 60° C. (140° F.) will be found quite sufficient for drying the damp granules; the stronger the alcohol used and the stiffer the paste made, the better will be the granular condition of the salt, especially if the subsequent drying can be conducted in drying-closets kept at a constant temperature.

All the required ingredients for effervescent granules must be used in fine powder and thoroughly mixed before an attempt at granulation is made; trituration in a mortar is not desirable, since the resulting pressure is likely to cause reaction between the sodium bicarbonate and acid, hence intimate admixture is best effected by passing the mingled powders repeatedly through a sieve (preferably No. 50). It will also be found advantageous to mix the sodium bicarbonate thoroughly with the sugar (if the latter is to be used) before adding the acid. Strong alcohol only should be used (not below 94 or 95 per cent. by volume) for making a paste that can be just rubbed through the sieve, otherwise the presence of much water will cause loss of carbon dioxide and yield a soft mass, which will not remain in separate granules while drying. The quantity of alcohol necessary will vary with the composition of the mixture; whenever citric acid or salts containing water of crystallization are present a lesser quantity should be used.

Well-tinned sieves must be used, through which the pasty mass is rubbed with the hands, otherwise the granules will not be perfectly white. A No. 6 or No. 8 sieve yields the most desirable size of granules, from which the fine particles, which are invariably formed along with the coarser, can be readily separated by shaking in a No. 20 or No. 30 sieve.

All effervescent powders should be preserved in well-stoppered bottles, in a dry place, as they are inclined to attract moisture from the air, and thus rapidly deteriorate.

EFFERVESCENT SALTS OF THE U. S. PHARMACOPŒIA.

Latin Name.	English Name.	Composition.	
Caffeina Citrata Effervescens	Effervescent Citrated Caffeine	Citrated Caffeine	40 Gm.
		Sodium Bicarbonate	570 "
		Tartaric Acid	300 "
		Citric Acid	195 "
Lithii Citras Effervescens	Effervescent Lithium Citrate	Lithium Citrate	50 Gm.
		Sodium Bicarbonate	570 "
		Tartaric Acid	300 "
		Citric Acid	195 "
Magnesii Sulphas Effervescens	Effervescent Magnesium Sulphate	Magnesium Sulphate	500 Gm.
		Sodium Bicarbonate	403 "
		Tartaric Acid	211 "
		Citric Acid	136 "

Effervescent Salts of the U. S. Pharmacopœia.—(*Continued.*)

Latin Name.	English Name.	Composition.
Potassii Citras Effervescens	Effervescent Potassium Citrate	Potassium Citrate . . . . 200 Gm. Sodium Bicarbonate . . 477 " Tartaric Acid . . . . . 252 " Citric Acid . . . . . . 162 "
Sodii Phosphas Effervescens	Effervescent Sodium Phosphate	Exsiccated Sodium Phosphate . . . . . . 200 Gm. Sodium Bicarbonate . . . 477 " Tartaric Acid . . . . . 250 " Citric Acid . . . . 162 "

SPECIAL REMARKS.

In all the above preparations careful observation of the official directions will lead to satisfactory results.

Effervescent Citrated Caffeine.—The present official effervescent citrated caffeine differs from former preparations in containing twice as much citrated caffeine, 4 per cent., and also in the total absence of sugar.

Effervescent Lithium Citrate.—This preparation is not identical with the one formerly recognized under that name; the latter occurred in form of a fine powder composed of lithium carbonate, citric acid, sodium bicarbonate, and sugar in suitable proportions, and when dissolved in water yielded an effervescent solution of lithium citrate. The quantity of lithium carbonate present was sufficient to produce nearly 9 per cent. of crystallized citrate, of which latter salt the present official preparation contains 5 per cent. Moreover, no sugar is now used in the granular salt.

Effervescent Magnesium Sulphate.—In the case of effervescent magnesium sulphate, a preliminary drying of the salt is necessary because magnesium sulphate contains over 50 per cent. of water of crystallization, the presence of which would render granulation impossible, or at least a very tedious operation; the Pharmacopœia therefore directs that the salt shall be heated on a water-bath until it ceases to lose weight, whereby about five-sixths of the water is removed. The nearly anhydrous salt is then reduced to powder and mixed with the other ingredients and granulated. Official magnesium sulphate represents about one-half its weight of the crystallized salt.

Effervescent Potassium Citrate.—While the former preparation of this name was simply a mixture of citric acid, potassium bicarbonate and sugar in such proportions that when dissolved in water a neutral salt would be produced, the present granular preparation contains 20 per cent. of potassium citrate, less than one-half as much as formerly, which is deprived of its water of crystallization, 5.55 per cent., before being mixed with the other ingredients. The sugar has likewise been omitted.

Effervescent Sodium Phosphate.—The object of directing the

CHAPTER XXXIII.

OINTMENTS AND CERATES.

Both classes of these preparations are intended solely for external application; they are of similar composition, of unctuous character, differing, however, from each other in degree of firmness and fusibility. While the U. S. Pharmacopœia officially recognizes the difference between ointments and cerates, this distinction is not maintained, as a rule, in Europe. The British and German Pharmacopœias designate both classes as ointments; in France the term *pommade* is applied to all ointments made with a purely fatty base, even if a small proportion of wax be present; while the term *onguent* is only used if a resinous or similar substance has been added, the name *cérat* being reserved for mixtures of fat and wax containing at least as much wax as our own cerates.

In the preparation of ointments and cerates it is of importance that perfectly smooth, homogeneous mixtures be obtained, and that the fatty vehicle be absolutely free from rancidity, since they are often applied to tender excoriated surfaces, and would otherwise prove a source of irritation instead of a soothing application. Lumps or gritty particles in ointments indicate unpardonable carelessness on the part of the dispenser.

Ointments and cerates made with yellow wax or resin are less liable to deterioration than when made with white wax, since the latter during the bleaching process undergoes incipient rancidity; they should be preserved in well-glazed, covered porcelain jars, and kept in a dry, moderately cool place. The true porcelain jars, although somewhat expensive, are to be preferred, as they are strictly impermeable to grease and can be thoroughly cleaned with hot water and lye whenever empty; the author had a set of these jars in constant use for over fifteen years without ever having an ointment turn rancid in them. Glass stock jars are offered at a much lower price, but will often crack while being cleaned, particularly with hot water, yet they are vastly superior to the ordinary white china or queensware covered jar, since the glazing of the latter soon becomes full of fine cracks, through which the fat permeates and, gradually turning rancid, contaminates the contents of the jar; moreover, no amount of washing will remove the rancid grease entirely from the pores of the jars, hence they soon become unfit for use. The sweet condition of ointments and cerates cannot be preserved without proper care and cleanliness; unfortunately these precautions are only too frequently disregarded by pharmacists.

OINTMENTS.

Ointments may be conveniently divided into distinct classes in regard to their therapeutic effect, thus: 1. Protective ointments, which are non-absorbable in character and act strictly epidermatically—that is, on the outer skin or cuticle. 2. Emollient ointments, which have nutritive or absorbefacient properties and act endermatically or by penetrating into the skin. 3. Ointments which produce systemic or constitutional effects, and must therefore be absorbable, penetrating not only into but through the skin. This difference in the therapeutic effects desired necessitates careful selection of the vehicle intended for exhibition of the medicinal agents. Non-absorbable ointments intended to produce some medicinal effect on the outer skin, such as astringent, counter-irritant, antiseptic, germicidal or similar effect, or possibly as protective agents, may therefore be made with petrolatum or a mixture of the same with hard paraffin, which latter combination is to be preferred in warm weather on account of its higher fusing-point. The British and German Pharmacopœias recognize such a vehicle under the name *unguentum paraffini*, which in the former case consists of hard paraffin 3 parts and soft paraffin 4 parts, and in the latter case of hard paraffin 1 part and liquid paraffin 7 parts; hence the British preparation is much the firmer of the two. For emollient ointments designed to penetrate into the skin for the purpose of producing a deeper local effect, such as anodyne, stimulant, resolvent, etc., preference should be given to lard, lard mixed with wax, lard and oil, oil and wax, or oil, wax, and spermaceti. As stated on page 206, the lard to be used for ointments should be free from water and other impurities. The absorbent properties of these bodies permit the admixture of medicinal agents in the form of solution either in water, alcohol, glycerin, oleic acid, or oil. In the last group of ointments, which are intended to produce systemic or constitutional effects, vehicles should be employed which penetrate not only into but through the skin, thereby permitting the absorption of the remedial agent present. No substance is known to possess these properties to a greater degree than wool fat and the modified form of the same, officially recognized under the name hydrous wool fat, and commonly designated as lanolin, which are themselves closely related to the fat secreted by the sebaceous glands of the human body. Wool fat can readily be combined with its own weight of water and even larger quantities, whereas lard takes up only about one-fifth of its weight of water and soft paraffins not more than 10 per cent.

The official glycerite of starch is sometimes used by physicians under the name of *plasma* or *plasma glycerini* as a vehicle for ointments in place of lard or petrolatum. It possesses the advantage of not being of a fatty nature, and hence easily removed by washing with water, and never becoming rancid; but as it is somewhat hygroscopic it must be preserved in well-closed jars. It is especially preferred by oculists for the application of lead acetate, mercuric oxide, and similar substances to the eyelids.

Dermatologists have long been looking for an ointment base or vehicle which, while non-irritating, should not be of a greasy nature if possible, so as to render its use more convenient and agreeable to patients. Numerous substances have been suggested, such as solvine or polysolve and oleite, which are alkali sulpho-ricinoleates, and as such miscible with water; gelatole, a mixture of oleite and gelatin, and similar semi-solid preparations, to be applied in the form of a thin layer or varnish-like coating. The most successful in this respect appears to have been a vehicle composed of casein, glycerin, and soft paraffin, which is used in Europe under the name *unguentum caseini.* According to Dr. Unna, the originator of this preparation, it is made by separating casein from milk, entirely deprived of its fat or cream, by addition of rennet at a temperature of about 35° C. (95° F.), collecting the curd, washing free from acid, and finally drying. Of the dried and powdered casein, 1400 parts are dissolved in 5000 parts of a weak alkaline solution, containing 34.5 parts of potassium hydroxide and 8.5 parts of sodium hydroxide. To this solution add 50 parts of carbolic acid and 700 parts of glycerin, and, when dissolved, 50 parts of zinc oxide and 2100 parts of vaselin are incorporated, and finally sufficient water is added to bring the total weight up to 10,000 parts. The finished preparation resembles very soft cold cream or thick condensed milk, is free from greasiness, and is said to be readily removed from the skin with water. Casein ointment is incompatible with acids and acid salts, but can be mixed with metallic mercury, tar, balsam of Peru, etc.; powdered vegetable or mineral substances should first be mixed with a little vaselin before incorporation.

As regards the mode of preparation of ointments, three distinct methods are followed, namely, by fusion, by incorporation of the medicinal agent with a suitable vehicle, and by chemical action. When ointments are to be made by fusion, those constituents having the highest fusing-point, as rosin, wax, and spermaceti, should be heated first, and, when nearly melted, the lard or oil added, bearing in mind that as long as some of the particles remain unmelted there is no danger from the continued application of heat, which should, however, be withdrawn in time to avoid a rise in temperature of the melted fats (see page 93). Fusion of ointments is preferably performed on a water-bath, in round-bottom pans or evaporating-dishes, and, if dirt be present, the melted mixture may be decanted, or, if necessary, strained through cheesecloth into a previously warmed dish or mortar; the liquid should then be stirred until a homogeneous soft mass results, after which it may be set aside and allowed to stiffen by further gradual cooling. The stirring of melted fats while cooling is essential to insure a perfectly smooth product, since fats are composed of solid and liquid bodies, which, during the cooling process, become partially separated, producing a granular solid on congealing, if allowed to cool at perfect rest, as may be seen in the case of plain lard; moreover, in a mixture of melted fats those having a higher fusing-point would naturally congeal earlier than the rest; therefore, unless an intimate mixture be kept up by constant stirring separation would ensue and a lumpy ointment result. The point of danger may be said to have been passed when the melted ointment, being continually stirred, has so far cooled that a uniform thick, creamy mass is obtained; for stirring, a broad wooden spatula will be found advantageous. When large quantities of aqueous liquids are to be incorporated with melted fats, as in the case of rose water ointment, the liquid should be warmed and then slowly added, with constant trituration, to the mixed fats previously somewhat cooled; otherwise the less fusible constituents will be chilled by the cold liquid and separate in granular form, thus preventing a smooth ointment. The following ointments are officially directed to be made by fusion:

Latin Name.	English Name.	Composition.	
Unguentum	Ointment	Benzoinated Lard	800 Gm.
		White Wax	200 "
Unguentum Aquæ Rosæ	Ointment of Rose Water (Cold Cream.)	Spermaceti	125 Gm.
		White Wax	120 "
		Expressed Oil of Almond	560 "
		Stronger Rose Water	190 "
		Sodium Borate	5 "
Unguentum Diachylon	Diachylon Ointment	Lead Plaster	500 Gm.
		Olive Oil	490 "
		Oil of Lavender	10 "
Unguentum Picis Liquidæ	Tar Ointment	Tar	500 Gm.
		Lard	350 "
		Yellow Wax	150 "
Unguentum Zinci Stearatis	Ointment of Zinc Stearate	Zinc Stearate	20 Gm.
		White Petrolatum	80 "

In the preparation of the official rose water ointment it is essential that a perfect solution of the borax in the rose water be effected, and to prevent sudden chilling of the fatty mixture the borax solution should be warmed somewhat. Constant stirring is necessary to produce a smooth, creamy ointment. The addition of borax to the official rose water ointment gives the latter a whiter and more creamy appearance, but at the same time interferes with the admixture of certain chemicals, such as calomel, yellow mercuric oxide, etc., causing discoloration of the ointment. Vegetable or mineral powders cannot be mixed in quantity with rose water ointment without forcing the water out of combination.

Unless the lead plaster for diachylon ointment be fresh, it is best to remove the darkened dry exterior, thus obtaining a lighter-colored and softer ointment; the oil must be added when the plaster is nearly melted on a water-bath, and a better mixture will result if the heat be continued for five or ten minutes afterward, so as to blend the oil and plaster more thoroughly. The melted mixture must be stirred until creamy, when the oil of lavender may be added, the whole transferred to a jar and allowed to cool. Diachylon ointment is preferably prepared fresh when wanted, as it does not keep well.

In preparing tar ointment, the tar should be free from granular matter and not incorporated with the mixture of lard and wax until the latter has been cooled to the condition of a smooth, soft ointment. If the tar be added to the hot liquid fats, a granular ointment will result.

Ointments prepared by incorporation of medicinal agents with an appropriate vehicle comprise by far the larger number of official ointments, and practically all those prescribed extemporaneously. The vehicles directed by the Pharmacopœia for the preparation of this class of ointments are lard, benzoinated lard, hydrous wool fat, petrolatum, and simple ointment; when absorption of the ointment is desired, wool fat or its hydrous modification is decidedly to be preferred. All substances to be mechanically incorporated in an ointment must be in the form either of solution or an impalpable powder; the latter condition, in the case of vegetable substances, can be attained only by passing the powder through a fine bolting-cloth sieve (about No. 120 or 150). The incorporation may be effected either in a mortar or on a heavy glass slab by means of a broad spatula, the finely powdered substance being first mixed with a small quantity of the vehicle, and, when a smooth mixture has been obtained, the remainder added; while an ointment slab is, as a rule, preferred in this country, the mortar is used almost exclusively in Europe, and for some ointments is in fact indispensable, particularly when solutions are to be added.

When the quantity of powder to be added is large, it will prove advantageous to melt some of the vehicle and mix this with the powder, in a warm mortar before adding the remainder. Some substances can be conveniently brought into a smooth condition by triturating with a little olive or expressed almond oil, such as calomel, lead carbonate, bismuth subnitrate, zinc oxide, etc., as well as certain crystallizable bodies, like mercuric chloride and silver nitrate; for the latter a little oil is decidedly better than water, since upon the gradual evaporation of the latter a return to the crystalline state is probable, giving rise to the presence of minute gritty particles which would cause irritation. Opium should be rubbed smooth with about an equal weight of water, and then at once incorporated with the fatty vehicle before the paste begins to dry. Some salts may be dissolved in water provided they are very soluble, as potassium iodide, while others must be reduced to an impalpable condition by trituration, as lead acetate, tartar emetic, zinc sulphate, etc. Red mercuric oxide, iodoform, naphthalene, and boric acid may be triturated with a few drops of alcohol, in a mortar, until rendered impalpable; camphor should be powdered, by the aid of alcohol, just before it is to be used, and added to the ointment after all other ingredients have been incorporated, since it is soluble in the fat and materially softens its consistence, which, in the case of solid extracts, would interfere considerably with their perfect admixture.

Whenever extracts such as belladonna, opium, stramonium, and the like, are to be exhibited in ointments, the pilular extracts are to

[illegible]

[illegible] small [illegible] water [illegible] the iodine [illegible] ment.

When iodine is ordered in conjunction with [illegible] ointment, the addition of potassium iodide is unnecessary, as a chemical reaction will take place between the [illegible] the proper plan would be to rub the iodine [illegible] and then add a portion of the mercurial ointment [illegible] until the color has disappeared and the change of color [illegible] then [illegible] taken place, after which the remainder of the ointment may be incorporated. If an extract, such as belladonna or stramonium, is to be added, this should be separately mixed with some of the fat and then added to the previous mixture, when a much better ointment will be obtained.

Substances which are wholly or partly soluble in fats, such as menthol, salol, chrysarobin, benzoic and carbolic acids, β-naphthol, and the like, should be triturated in fine powder form with a portion of the vehicle liquefied by heat, and after addition of the remainder, the mixture must be continually stirred until cool. If hydrated chloral, thymol, naphthol [illegible] ordered in conjunction with camphor, in an ointment, the two substances must be triturated together until an oily fluid results, which can then be readily incorporated with the vehicle.

Alkaloidal salts may be incorporated in ointments [illegible] solution in water or, if present in large quantity, may be mixed in the form of a very fine powder; but whenever pure alkaloids are ordered by physicians these should be triturated with [illegible] quantity of warm oleic acid before they are mixed with the base, [illegible] a more intimate distribution is [illegible] obtained than [illegible] merely rubbed into a smooth paste [illegible] means.

Glycerin should never be used in place of oil or water to produce a smooth paste with vegetable or mineral powders, because, although derived from fats, it can be incorporated with them permanently only with difficulty. When glycerin in considerable quantity is ordered to be added to an ointment consisting chiefly of lard or a mixture of lard or oil with wax, the addition of a small proportion of anhydrous wool fat, in place of a like quantity of the regular vehicle, will overcome all difficulty of incorporation. A similar expedient will prove most valuable when large quantities of aqueous fluids are to be incorporated in ointments, or in the case of alcoholic liquids, which ordinarily mix with fats with great difficulty. The pharmacist, in preparing ointments containing fluids, must so combine the constituents that a permanent homogeneous mixture results, from which the fluids will not separate on standing.

It will be found very convenient to keep on hand anhydrous wool fat for the purposes above stated; it is readily prepared by heating some of the commercial lanolin (containing about 30 per cent. of water) on a water-bath until it ceases to lose weight.

When two or more ointments having different fusing-points are to be mixed, the firmer should always be rubbed down by itself first, and the softer fats then be incorporated in small quantities at a time, otherwise an imperfect mixture results. A mixture of mercurial ointment with lard or simple ointment offers an example; in cold weather this mode of procedure is all the more imperative; it should also be followed when anhydrous wool fat is to be mixed with softer fats, as the former is usually somewhat tough.

Whenever substances likely to attack metal are ordered in ointments, the incorporation with the fatty vehicle should never be made with steel spatulas, but always with horn or rubber-coated ones; the latter can now be had quite pliable, and are admirably adapted for ointments containing salicylic acid, tannic acid, iodine, mercuric chloride, etc.

The Pharmacopœia directs the following 18 ointments to be prepared by incorporation of the medicinal agent with the fatty vehicle.

Latin Name.	English Name.	Composition.	
Unguentum—			
Acidi Borici . . .	Boric Acid Ointment .	Boric Acid	100 Gm.
		Paraffin	100 “
		White Petrolatum	800 “
Acidi Tannici . . .	Tannic Acid Ointment	Tannic acid	20 Gm.
		Glycerin	20 “
		Ointment	60 “
Belladonnæ	Belladonna Ointment	Extract of Belladonna Leaves,	10 Gm.
		Diluted Alcohol	5 Cc.
		Hydrous Wool Fat	20 Gm.
		Benzoinated Lard	65 “
Chrysarobini . . .	Chrysarobin Ointment	Chrysarobin	6 Gm.
		Benzoinated Lard	95 “
Gallæ	Nutgall Ointment . .	Nutgall, in No. 80 powder,	20 Gm.
		Ointment	80 “

Latin Name.	English Name.	Composition.	
Unguentum—			
Hydrargyri . . .	Mercurial Ointment .	Mercury	500 Gm.
		Lard	250 "
		Prepared Suet	230 "
		Oleate of Mercury	20 "
Hydrargyri Ammoniati	Ointment of Ammoniated Mercury . . .	Ammoniated Mercury . .	10 Gm.
		Hydrous Wool Fat	40 "
		White Petrolatum	50 "
Hydrargyri Dilutum	Blue Ointment . . .	Mercurial Ointment . . .	670 Gm.
		Petrolatum	330 "
Hydrargyri Oxidi Flavi . . .	Ointment of Yellow Oxide of Mercury .	Yellow Mercuric Oxide .	10 Gm.
		Water	10 "
		Hydrous Wool Fat	40 "
		Petrolatum	40 "
Hydrargyri Oxidi Rubri . . .	Ointment of Red Oxide of Mercury . . .	Red Mercuric Oxide	10 Gm.
		Water	10 "
		Hydrous Wool Fat . . .	40 "
		Petrolatum	40 "
Iodi	Iodine Ointment . .	Iodine	4 Gm.
		Potassium Iodide . . .	4 "
		Glycerin . .	12 "
		Benzoinated Lard	80 "
Iodoformi . .	Iodoform Ointment	Iodoform in very fine powder	10 Gm.
		Lard	90 "
Phenolis	Ointment of Phenol (Carbolic Acid Ointment	Phenol	3 Gm.
		White Petrolatum	97 "
Potassii Iodidi	Ointment of Potassium Iodide	Potassium Iodide . . .	10 Gm.
		Potassium Carbonate	0.6 "
		Water	10 "
		Benzoinated Lard . .	80 "
Stramonii .	Stramonium Ointment	Extract of Stramonium . .	10 Gm.
		Diluted Alcohol .	5 "
		Hydrous Wool Fat . .	20 "
		Benzoinated Lard .	65 "
Sulphuris .	Sulphur Ointment	Washed Sulphur	15 Gm.
		Benzoinated Lard .	85 "
Veratrinæ	Veratrine Ointment	Veratrine	4 Gm.
		Expressed Oil of Almond	6 "
		Benzoinated Lard	90 "
Zinci Oxidi	Ointment of Oxide of Zinc . . .	Zinc Oxide .	20 Gm.
		Benzoinated Lard	80 "

The official directions accompanying each formula and the general directions given above are sufficiently explicit to insure satisfactory ointments, therefore further comment is unnecessary except in two or three cases.

The extinguishment of mercury by means of [illegible] of mercury, in the preparation of mercurial ointment, is readily effected by trituration in a mortar on a small scale, but on a large scale it is [illegible] follow the plan of prolonged agitation [illegible]. When the globules of mercury [illegible] the mixture of lard and suet, melted and partly cooled [illegible] incorporated. The Pharmacopœia demands that the ointment, when assayed by dissolving all the fatty matter [illegible] benzin and weighing the [illegible] shall yield not less than 48 per cent. of mercury. [illegible] mercurial ointment may become almost liquid and is then liable to lose mercury by separation, hence the necessity for keeping it in a cool place. When mercurial ointment is prescribed in divided doses by physicians, each portion should be separately weighed on paraffin or parchment paper, and then folded as directed in the chapter on Powders.

The present official Blue Ointment (Unguentum Hydrargyri Dilutum, U. S. P.) corresponds in mercurial strength to the preparation formerly known as Mild Mercurial Ointment (Unguentum Hydrargyri Mite), containing ⅓ of its weight of metallic mercury. It should not be used in prescriptions unless specially designated.

In the case of the ointments of red and yellow mercuric oxide, trituration of the oxide with distilled water is directed for the purpose of insuring reduction to an impalpably fine condition, and the hydrous wool fat facilitates the incorporation of the petrolatum in the presence of the water. Only glass, porcelain, or horn utensils should be used, and the ointment should be protected against direct sunlight and high temperatures.

The addition of potassium carbonate to ointment of potassium iodide is for the purpose of preserving its white appearance; without this addition (or that of sodium thiosulphate, as ordered by the German Pharmacopœia) the ointment will gradually turn yellow and finally brownish, owing to slow liberation of iodine. This discoloration is due to decomposition of the potassium iodide, said to be due to formation of hydrogen dioxide by the action of light on the water present; formerly the decomposition was thought to be due to the action of fatty acids.

Of the ointments made by chemical action, the official ointment of mercuric nitrate is a striking example. It is made by heating 760 Gm. of lard to a temperature of 105° C. (221° F.), then withdrawing the heat and gradually adding 70 Gm. of nitric acid. When the reaction moderates, heat is again applied until effervescence ceases. Having dissolved 70 Gm. of mercury in 105 Gm. of nitric acid, the clear solution is added to the lard mixture, which has been allowed to cool to 40° C. (104° F.), and the whole thoroughly mixed until cold by means of a porcelain or wooden spatula. When lard is heated and mixed with nitric acid, the former undergoes oxidation at the expense of the acid, olein being converted into a new compound, solid at ordinary temperatures, known as elaidin, the term olein being usually applied to the fluid constituent of fats and fixed oils. The incorporation of the solution of mercuric nitrate subsequently with the elaidin is simply a mechanical admixture, the solution having no chemical effect whatever on the fat. It is essential that the nitric acid be of official strength, and that heat be reapplied, if necessary, to complete the oxidation of the fat; care should be taken that the temperature above indicated be not exceeded, as over a direct fire decomposition of the fat is likely to ensue and a dark-brown compound result if too high a heat be applied. The temperature of a boiling-water bath is usually quite sufficient to bring about the desired reaction, although this method requires a little more time. The oxidation of the lard goes on quietly, and is known to be ended when effervescence ceases and a soft, solid mass is obtained upon cooling. The solution of mercury in nitric acid can be made in the cold, and may be warmed finally to expel any colored gas that has been retained. If the fat has been properly oxidized and cooled, as directed in the Pharmacopœia, a bright lemon-yellow ointment will result; but if the oxidation of the lard has not been completed before addition of the solution of mercuric nitrate, owing either to the use of weak nitric acid or insufficient heat, decomposition of the metallic salt will result in order to satisfy the avidity of the fat, and the ointment will assume a dark color. Ointment of mercuric nitrate is also known as *citrine ointment* and its official Latin title is *unguentum hydrargyri nitratis.* It should never be brought into contact with metal.

Another instance of chemical reaction in the preparation of ointments is in the original formula for Hebra's ointment: lead oxide is heated with olive oil in the presence of water until all the oxide has chemically combined with the fatty acids derived from decomposition of the oil, the newly formed lead oleate remaining intimately mixed with the excess of oil and the glycerin liberated from the fat. The decomposition taking place will be more fully explained under the head of Saponification, in Part III. The original Hebra's ointment differs from the official diachylon ointment in containing some free glycerin.

Ointments should always be dispensed in glass or porcelain jars provided with suitable covers; if the latter be of metal or wood, a disk of heavy paraffin paper should be inserted, to avoid contact with the fatty substance. Under no circumstances, *except when intended for immediate use*, should ointments be put up in wood boxes, as the fat will readily penetrate the material, and thus become exposed to oxidation by the air. When ointment jars are returned to be refilled, they should be carefully wiped out with soft paper and washed thoroughly before the new ointment is put in; a fresh disk of paraffin paper should also be inserted, and a new label be put on the jar if the old one has become soiled.

To cleanse the apparatus in or on which ointments have been prepared, the best plan is first to wipe off all remaining grease with clean sawdust or soft paper, and then to wash it well with warm water and lye or soap. In the case of iodoform ointment a few drops of oil of turpentine will remove the characteristic odor readily, as stated on page 348.

CERATES.

This class of preparations differs from ointments in containing a considerable proportion of wax, and frequently also rosin or oleoresinous substances. Cerates are intended to be applied as dressings, usually spread on linen or soft leather; while they become somewhat softer at the temperature of the body, they do not liquefy, and are intended to act only locally as protective, cooling, astringent, stimulating, or blistering agents. What has been said before regarding the preparation of ointments by fusion, and also their preservation, applies likewise to cerates; owing to their firm consistence the latter are not well adapted to admixture with powdered substances, although fluids are sometimes incorporated with them.

The Pharmacopœia recognizes 6 cerates, which, with the exception of the cerate of lead subacetate, are usually carried in stock by the pharmacist. Three of the official cerates contain rosin, and, in these, yellow wax also is used; hence they will not become rancid. Of the remaining three, two are made with white wax, petrolatum, and benzoinated lard, and one with paraffin, petrolatum, and wool fat.

The following is a list of the official cerates, showing their composition:

Latin Name.	English Name.	Composition.	
Ceratum	Cerate	White Wax	300 Gm.
		White Petrolatum	200 "
		Benzoinated Lard	500 "
Ceratum Camphoræ	Camphor Cerate	Camphor Liniment	100 Gm.
		White Wax	350 "
		White Petrolatum	150 "
		Benzoinated Lard	400 "
Ceratum Cantharidis	Cantharides Cerate	Powdered Cantharides	320 Gm.
		Liquid Petrolatum	150 "
		Yellow Wax	180 "
		Rosin	180 "
		Lard	170 "
Ceratum Plumbi Subacetatis	Cerate of Lead Subacetate (Goulard's Cerate)	Solution of Lead Subacetate	20 Gm.
		Wool Fat	20 "
		Paraffin	20 "
		White Petrolatum	38 "
		Camphor	2 "
Ceratum Resinæ	Rosin Cerate (Basilicon Ointment)	Rosin	350 Gm.
		Yellow Wax	150 "
		Lard	500 "
Ceratum Resinæ Compositum	Compound Rosin Cerate	Rosin	225 Gm.
		Yellow Wax	225 "
		Prepared Suet	300 "
		Turpentine	115 "
		Linseed Oil	135 "

Camphor cerate and Goulard's cerate both contain 2 per cent. of camphor, which would seem hardly sufficient to impart marked medicinal properties to the preparations.

In the formula for cerate of cantharides the object of macerating the powdered cantharides for 48 hours in a warm place with about half their weight of liquid petrolatum is to facilitate the subsequent solution of cantharidin in the fats, since petrolatum is known to exert a solvent effect upon the blistering principle. The official process always insures an efficient blistering cerate, provided the cantharides are of good quality. In order to prevent the separation of the powder from the melted fats, it is important that the mixture, after removal from the water-bath, be constantly stirred until it begins to congeal. In Great Britain, Germany, and France this cerate is known as *emplastrum cantharidis* or *emplastrum vesicans;* in some localities it is also designated as *emplastrum lyttæ.*

The official rosin cerate congeals as a perfectly homogeneous mixture upon cooling without stirring, on account of the large proportion of rosin and wax present; stirring of the melted and strained mixture is, in fact, not desirable in this case, as it incorporates considerable air. Rosin cerate gradually grows tougher by age. In cold weather the proportions of lard and yellow wax may be changed with advantage to lard 530 Gm. and yellow wax 120 Gm. in the official formula.

Compound rosin cerate is often called for under the name Deshler's salve. If kept on hand for some time it becomes tough, which condition may be avoided by using olive oil or liquid petrolatum in place of the linseed oil.

Of late years both ointments and cerates have been largely superseded, especially in Europe, by *dermatologic pastes and glycerogelatins.* The former are mixtures of the medicinal agents with starch, dextrin, or kaolin, and glycerin, soft soap, petrolatum, or lard, and are intended chiefly for antiseptic, astringent, or germicidal effects. As a general vehicle for the preparation of these pastes, a mixture of dextrin, glycerin, and distilled water, equal parts by weight, may be brought into solution with the aid of heat, and sufficient water finally added to restore any loss by evaporation. Ichthyol, naphthol, resorcin, salicylic acid, sulphur, and zinc oxide are the more important remedial agents used in the form of pastes, the proportions being varied to suit particular cases. The glycerogelatins are firmer than the pastes, and must be melted before they can be applied to the affected parts, which latter is done by means of a soft brush. The vehicle consists of a mixture of gelatin, glycerin, and water, made in proportions ranging from 5, 20, and 65 parts to 15, 45, and 25 parts of the respective constituents. As medicating agents, chrysarobin, ichthyol, iodoform, resorcin, salicylic acid, and zinc oxide are added singly or in combination.

Another form of modern dermic medication is by means of *pencils*, of which the following formula serves as an example: salicylic acid 10 parts, powdered tragacanth 5 parts, starch 30 parts, dextrin 35 parts, sugar 20 parts, glycerin and water sufficient to make a paste, which is rolled out into rods about 7 millimeters (¼ inch) in diameter and 5 centimeters (2 inches) in length. The pencils are dried at ordinary temperature on parchment paper and wrapped in tinfoil.

The official kaolin poultice, Cataplasma Kaolini, is often used in place of ointments as a soothing protective dressing. It is made by mixing finely powdered boric acid 45 Gm. with finely powdered kaolin previously heated for an hour with frequent stirring on a boiling-water bath 577 Gm., then incorporating the mixed powders with glycerin 375 Gm., and finally adding thymol 0.5 Gm., oil of peppermint 0.5 Gm., and methyl salicylate 2 Gm. This cataplasm is a stone-colored homogeneous mass, which should be preserved in air-tight containers on account of its tendency to absorb moisture from the air.

CHAPTER XXXIV.

LINIMENTS AND OLEATES.

THESE preparations are closely allied to those described in the preceding chapter, being also intended only for external use.

LINIMENTS.

Liniments are fluid or semifluid preparations, usually in the form of solutions, although in some instances merely mechanical mixtures, the solvent or vehicle being either a fixed or volatile oil or alcohol, which latter is sometimes mixed with water. They are always applied to the skin with friction, and, when mechanical mixtures only, require to be well agitated before they are applied. For endermatic medication liniments are in many cases to be preferred to ointments, because, being applied with friction, the medicinal agents are more likely to be readily absorbed by the unbroken skin. For this purpose it is essential that the vehicle be of a volatile or fatty character, since non-volatile substances in aqueous solution are either not absorbed at all or only to a slight extent, while the same substances dissolved in alcohol, chloroform, or ether are quickly taken up, as shown by their prompt appearance in the secretions. The Pharmacopœia recognizes 8 liniments, of which 4 are of a fatty nature, while 4 are alcoholic or hydro-alcoholic solutions; with 2 exceptions, they are usually prepared extemporaneously, although they keep well.

When fixed oils are shaken with aqueous solutions of alkalies, partial decomposition of the fat takes place, and an emulsion-like mixture results, in which the remaining oil is kept in perfect suspension by the newly formed soap; such liniments thicken considerably by age, which it is intended to provide against in the official formula for ammonia liniment by the addition of alcohol. If the fixed oils used are fresh and perfectly sweet, they are but little acted on by alkalies in the cold, hence the preparation of a perfect liniment becomes difficult.

The following is a list of the official liniments:

Latin Name.	English Name.	Composition.	
Linimentum Ammoniæ	Ammonia Liniment . (Volatile Liniment.) (Hartshorn Liniment.)	Ammonia Water	350 Cc.
		Alcohol	50 "
		Cottonseed Oil	570 "
		Oleic Acid	30 "

Latin Name.	English Name.	Composition.	
Linimentum Belladonnæ	Belladonna Liniment	Camphor Fluidextract of Belladonna Root, sufficient to make	50 Gm. 1000 Cc.
Linimentum Calcis	Lime Liniment (Carron Oil.)	Lime Water Linseed Oil } of each	500 Cc.
Linimentum Camphoræ	Camphor Liniment	Camphor Cottonseed Oil	200 Gm. 800 "
Linimentum Chloroformi	Chloroform Liniment	Chloroform Soap Liniment	300 Cc. 700 "
Linimentum Saponis	Soap Liniment (Liquid Opodeldoc.)	Powdered Soap Camphor Oil of Rosemary Alcohol Water sufficient to make	60 Gm. 45 " 10 Cc. 725 " 1000 "
Linimentum Saponis Mollis (Tinctura Saponis Viridis.)	Liniment of Soft Soap (Tincture of Green Soap.)	Soft Soap Oil of Lavender Alcohol sufficient to make	650 Gm. 20 Cc. 1000 "
Linimentum Terebinthinæ	Turpentine Liniment	Rosin Cerate Oil of Turpentine	650 Gm. 350 "

SPECIAL REMARKS.

The use of cottonseed oil alone for the preparation of ammonia liniment has not been satisfactory, separation into two distinct layers invariably occurring in the mixture, and while the addition of about 20 per cent. of common olive oil for a like quantity of the cottonseed oil was found to improve the condition on account of the free fatty acids generally present in the lower grades of olive oil, the present official formula directing the addition of a small quantity of oleic acid is preferable. The acid unites with the ammonia, forming a soap, ammonium oleate, which materially aids in emulsionizing the cottonseed oil. The presence of 5 per cent. of alcohol is intended to prevent undue thickening of the liniment if kept on hand for some time.

In the preparation of camphor liniment, the solution of the camphor can be materially hastened by placing it, with the oil, in a strong bottle and, after corking the same securely, digesting the mixture on a water-bath at a moderate heat.

The official belladonna liniment is decidedly the most efficient preparation of that drug for external use, but owing to its potent character and ready absorbability serious results may occur from its liberal use. Both the alcohol and camphor aid absorption, and it should never be dispensed except on a physician's prescription.

The chloroform liniment of the United States Pharmacopœia differs materially from that of the British Pharmacopœia; the latter is a mixture of equal volumes of chloroform and camphor liniment. A very popular preparation, known as Compound Chloroform Liniment, is composed of 1 volume each of chloroform and tincture of aconite and 6 volumes of soap liniment.

Dried soap, as directed in the Pharmacopœia, is to be much preferred in making soap liniment, on account of the variable quantity of moisture present in the official soap. The present official directions yield a very satisfactory product with little expenditure of time. The soap is readily dissolved in the boiling water, and if the alcohol be added to the gelatinous mass, while the latter is still warm, a clear solution is obtained very soon. The official directions to set the liniment aside in a cool place for twenty-four hours, and then to filter, are for the purpose of getting rid of the sodium palmitate always present in Castile soap, which is but sparingly soluble in the menstruum, particularly in the cold.

The official turpentine liniment is also known as "Kentish" liniment; only a moderate heat should be employed to melt the rosin cerate, so as to avoid volatilization of the oil of turpentine, which must also be added in small quantities, with constant stirring, until a smooth, uniform, opaque mixture results.

Closely allied to the liniments are the *infused oils*, made by digesting 20 Gm. of an alkaloidal drug, previously macerated with ammoniated alcohol, with a mixture of 50 Cc. each of cottonseed oil and lard oil until the alcohol has been vaporized. The active principles of the drug are intended to be taken up by the oils, together with green coloring-matter.

The so-called *drying liniments* or *medicated varnishes* consist of mucilage of tragacanth, starch or dextrin, with egg-albumen, suitably medicated, which when applied to the skin leave a thin varnish or protective film, similar to that obtained with collodion.

OLEATES.

This class of preparations has been in use by physicians in this country since 1872. Normal oleates are true chemical compounds of oleic acid with metallic oxides or alkaloids, but the oleates medicinally employed are simply mixtures of such normal oleates with oleic acid or some other diluent. The proportion of any particular metallic oxide or alkaloid to be dissolved in oleic acid may vary with the views of the physician; but in the case of normal oleates a certain proportion cannot be exceeded. The expressions 2, 5, 10, or 20 per cent. oleate are used to indicate that 2, 5, 10, or 20 parts of the respective alkaloid or metallic oxide are present in every 100 parts of the finished product. The following table shows the amount of base combined with oleic acid in 100 parts of the respective normal oleates:

Normal	Oleate of	Iron (ferric)	8.8	per cent.	of	anhydrous ferric oxide.
"	"	Copper	12.7	"	"	cupric oxide.
"	"	Zinc	12.9	"	"	zinc "
"	"	Bismuth	22.0	"	"	bismuth "
"	"	Mercury	28.4	"	"	mercuric "
"	"	Lead	28.9	"	"	lead "
"	"	Morphine	50.3	"	"	morphine.

Normal Oleate of	[illegible]	[illegible]	[illegible]
" "	[illegible]	[illegible]	[illegible]
" "	[illegible]	[illegible]	[illegible]
" "	[illegible]	[illegible]	[illegible]
"	[illegible]	[illegible]	[illegible]

From these [illegible] made by [illegible] lowing [illegible]

[illegible]

is 1 ounce of dry soap to the pint. Purer metallic oleates can be obtained by using a solution of sodium oleate made directly from official oleic acid by the following process: Warm, in a capacious dish, 1217 grains of oleic acid to about 60° or 65° C. (140° or 149° F.) and add slowly 192 grains of sodium hydroxide (90 per cent.) dissolved in a mixture of 2 fluidounces of distilled water and 6 fluidrachms of alcohol, stirring constantly until the acid is neutralized, which is best ascertained by testing a small portion of the resulting soap, dissolved in alcohol, with a few drops of phenolphtalein solution—not more than a faint pink tint should appear. The soap is next dissolved in 3 pints of water and filtered. A solution of potassium oleate of about the same strength may be obtained if to 1 pint of boiling water be added 410 grains of potassium bicarbonate and afterward 1156 grains of oleic acid, the mixture being boiled until the acid has all been taken up and a clear soap solution results, which, when cold, is diluted to 3 pints by addition of water. To 1 pint of either of these alkali oleate solutions may be added ½ pint of a metallic salt solution containing the following quantities of the salt:

For 1 pint of sodium oleate solution:

Lead Acetate, crystallized	273 grains.
Copper Sulphate, crystallized	180 “
Zinc Sulphate, crystallized	207 “
Mercuric Nitrate	237 “

For 1 pint of potassium oleate solution:

Lead Acetate, crystallized	259 grains.
Copper Sulphate, crystallized	170 “
Zinc Sulphate, crystallized	197 “
Mercuric Nitrate	225 “

The United States Pharmacopœia recognizes 5 oleates, all made by direct solution of the active ingredient in oleic acid; they are:

Oleate of atropine, containing 2 per cent. of atropine; oleate of cocaine, containing 5 per cent. of cocaine; oleate of mercury, containing 25 per cent. of mercuric oxide; oleate of quinine, containing 25 per cent. of quinine; oleate of veratrine, containing 2 per cent. of veratrine. With the exception of the oleate of mercury, which is of the consistence of firm butter, the official oleates are all liquid, being solutions of the respective oleates in an excess of oleic acid, combined in the case of the oleates of atropine, cocaine, and veratrine with about an equal volume of olive oil. The Pharmacopœia directs the alkaloids atropine and cocaine to be triturated with about an equal weight of alcohol, and the yellow mercuric oxide with an equal weight of distilled water, before addition of the oleic acid, in order to facilitate solution, the alcohol and the water being subsequently driven off by means of heat.

Powdered oleate of zinc should be the true normal oleate, but the commercial article is frequently mixed with an excess of zinc oxide;

it is best prepared by the process suggested by Mr. Beringer, which is as follows: warm the sodium oleate solution (see above) to 43° C. (109.4° F.), and add slowly, with constant stirring, the solution of zinc sulphate, collect the precipitate on a moist filter, wash thoroughly with water, and dry, on porous paper, at a temperature not above 38° C. (100° F.). In order that the oleate, when dry, may be obtained in white friable masses which can easily be passed through a sieve as an impalpable unctuous powder, it is important that the temperature during precipitation be maintained between 38° and 43° C. (100.4° to 109.4° F.).

Under the names of ointments of the various oleates, manufacturers have for some time offered a class of preparations in regard to which some confusion exists, as the vehicle as well as the proportion of the oleate used varies with different manufacturers; the vehicle is either benzoinated lard or soft or firm petrolatum, hence the consistence may vary considerably. The term "ointment of any oleate, 5, 10, or 20 per cent.," can have but one meaning as far as the active ingredient is concerned, namely, that the finished product contains 5, 10, or 20 parts of the respective normal oleate in every 100 parts of the ointment, and not 5, 10, or 20 parts of the alkaloid or metallic oxide, as is frequently supposed. Ointments of oleates have received official recognition in two instances, the ointment of mercuric oleate and the ointment of zinc oleate, both of the British Pharmacopœia, the former containing 25 per cent. of normal mercuric oleate and the latter 50 per cent. of normal zinc oleate. Besides these the ointments of aconitine, atropine, and veratrine of the same Pharmacopœia must be looked upon as ointments of oleates, since the respective alkaloids are dissolved in an excess of oleic acid before incorporation with the lard.

CHAPTER XXXV.

PLASTERS AND SUPPOSITORIES.

PLASTERS.

PLASTERS are preparations intended for external application, which, although firmer and more tenacious than cerates, become adhesive by the heat of the body, and may be made to serve the purpose of offering both support and medication to the parts to which they are applied. They are firm solids at ordinary temperature and cannot be spread without the aid of heat, but retain a certain degree of flexibility when applied to the body. The base or mass of nearly all the official plasters is either simple lead plaster or a mixture of the same with wax, rosin, and gum-resins; in large manufactories a rubber-mass is specially prepared from caoutchouc and certain aromatic resins and vegetable powders, which is to be preferred in some cases on account of its flexibility and adhesiveness. In the preparation of the rubber plaster-base the crude India rubber of commerce is first freed from impurities, by steaming and continuous washing with warm water in suitable machinery until all foreign matter has been removed, after which it is repeatedly passed between heavy steel rollers kept at a temperature of about 35° or 37° C. (95° or 98.6° F.); during this kneading process the rubber gradually softens and assumes a plastic condition which fits it admirably for the incorporation of very finely powdered olibanum, orris root, and rosin or Burgundy pitch, this being also effected between warm smooth rollers.

Some authorities contend that plasters made with a rubber base are wholly inefficient where systemic or even endermatic effects are desired, since, as they claim, the rubber combination does not permit the release and subsequent absorption of the medicinal agent present. Opinions are divided on this point, and while there is no doubt that a volatile or a fatty vehicle will permit the absorption of any medicinal agent in admixture more readily than an insoluble mass of rubber, rosin and wax, or lead oleate, many physicians claim to have observed positive good effects from rubber-base plasters, and the testimony of many hundred laymen is in favor of this decidedly more pleasant and convenient form of plasters.

As in the case of ointments, plasters may be divided into three groups with regard to their therapeutic action:

1. Plasters intended to exercise a supportive, protective, antiseptic, counterirritant, or vesicant effect. These will act only epidermatically, and a mass possessing the property of ready and continued

adhesiveness is to be preferred; hence the official adhesive plaster and similar rubber combinations are well adapted for this group, as they possess the advantage of greater adhesiveness, especially in the presence of moisture.

2. Plasters intended to produce an endermatic effect, such as anodyne, astringent, alterative, sedative, or stimulant. This group includes the official plasters of belladonna, lead, opium, and soap; and while lead oleate, together with its admixtures of rosin or soap, is preferred by many as a vehicle, it is safe to assume that the large quantities of plasters of this group made with rubber-mass are used not without good results.

3. Plasters intended for constitutional and systemic effects. As these require penetration not only into but through the skin, it is absolutely necessary that the vehicle be one of recognized absorbability: the only official representative of this group is mercurial plaster, and it is very doubtful whether this is not decidedly inferior to mercurial plaster-mull or salve-mull, now preferred by physicians, and often prescribed as steatinum hydrargyri or unguentum hydrargyri extensum (see page 434).

The preparation of plaster-masses by pharmacists is very similar to that of cerates, being preferably conducted with water-bath heat, those constituents having the highest fusing-point being first introduced into the pan or dish, and others of greater fusibility being gradually incorporated. All wholly or partly volatile substances, as oleoresins or essential oils, must be added last, and non-fusible substances must be incorporated in the form of very fine powder whenever possible; as gum-resins are frequently added to plaster mixtures, and as they cannot be reduced to fine powder without injury, they must either be treated in coarse powder with alcohol, and the resulting solution of resinous matter then evaporated to a syrupy consistence, as in the case of asafetida, myrrh, and galbanum, or be emulsionized with diluted acetic acid and then evaporated until the liquid hardens on cooling, as in the case of ammoniac. In either case the concentrated liquid should be added to the fused mixture when it begins to cool, the mass being well stirred to insure uniform distribution.

Fluid and solid extracts must be incorporated as in the case of ointments, the former after evaporation to a syrupy consistence, the latter after softening with a little water or diluted alcohol, as the case may be. As in the case of ointments, the extinguishment of metallic mercury in plasters is most conveniently effected by trituration with mercuric oleate.

If any foreign matter, such as sand, pieces of wood, and the like, should be found in the melted plaster, this is best removed by decantation or straining, which must always be done before the insoluble and non-fusible substances are added; if straining be resorted to, it will be advisable to perform this operation with the smallest bulk possible, the strained material being always received in a warm pan or dish.

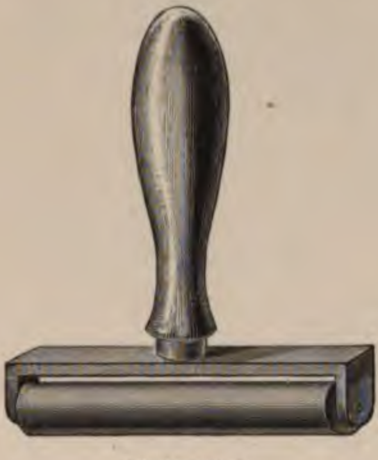
If plasters are to be preserved for stock, they are usually rolled into cylindrical pieces of convenient thickness weighing about 4 or 8 oz.; this operation is performed on a slab or board previously moistened with water or expressed oil of almond; these sticks or rolls should be wrapped in waxed or paraffin paper to protect them from the air.

Although, with one exception, the term plaster is officially applied to the mass or combination to be spread upon leather or muslin, it is more extensively used in trade to designate the finished spread plaster, ready for application. The spreading of plasters has almost entirely passed out of the hands of pharmacists, hence it does not now appear necessary to describe and illustrate the various appliances which twenty-five or thirty years ago were considered a very essential and important part of every educated pharmacist's outfit. Plaster-masses, official and otherwise, can now be purchased of reliable quality, spread on muslin or other material, in one- and five-yard rolls, or in definite and convenient sizes, from large manufacturers, and there is to-day no more reason why a pharmacist should make and spread belladonna plasters than that he should return to the spreading of adhesive plaster, as was done many years ago. Moreover, plasters are prescribed but rarely now by physicians, and, when some new combination is ordered, the pharmacist will probably have little difficulty in spreading a plaster of fair quality and appearance by following the few general directions here given.

For extemporaneously spread plasters the best material is soft white leather, the kind known in the trade as plaster skin. A piece should be cut 1 inch larger each way than the size of the plaster ordered; thus a 4 x 6 plaster would require a piece of leather 5 x 7 inches; now prepare 4 strips, $\frac{1}{2}$ inch in width, of stiff paper, preferably glazed, and having previously prepared the plaster-mass on a water-bath, as directed above, apply the paper strips to the rough side of the plaster skin in such a manner that the desired space shall remain uncovered, and carefully pour the melted plaster on the leather, smoothing the surface with a warm spatula, or by holding the spread plaster near a stove or furnace-register and allowing the soft material to run smooth. Then, having placed the spread plaster on a level surface, with a quick motion remove the paper strips before the plaster surface hardens, so that a clean half-inch margin around the plaster proper may be obtained. In place of a spatula, the roller shown in Fig. 268 may be used with advantage for smoothing the spread plaster-mass; it should be dipped in hot water, so as to become warm, before it is used, and then be moistened with a mixture of 1 volume of glycerin and 2 volumes of water to prevent adhesion.

If the paper strips be attached before the melted mass is ready to be applied, the paste is likely to dry out, when subsequent removal of the paper from the rough leather becomes difficult, and hence some pharmacists prefer to moisten the strips with a damp sponge just previous to spreading the plaster-mass; this plan has been found very advantageous. Instead of using paper strips, some prefer to cut a frame of thin cardboard, with a central opening of the required shape and size of the plaster, which is tacked down on the plaster skin. The amount of material necessary for spreading a plaster of the required thickness need not exceed 12 or 15 grains for each square inch, or about 0.165 Gm. for each square centimeter. Plaster-spreading requires manipulative skill, and practice alone can bring success; yet the writer has seen some plasters spread by students in his laboratory, who had never before seen the operation, that would have been a credit to any first-class pharmacy.

FIG. 268.



Plaster-roller.

Mammary or breast plasters are always made circular in form, about 8 inches in diameter, with a 1-inch margin; a hole 1½ inches in diameter is cut in the centre, and from this point to the outer edge the plaster is slit to admit folding over the breast. Such plasters are preferably spread on chamois skin, which is softer.

Fly-plaster is the name frequently applied to cantharides or blistering cerate when the same has been spread upon adhesive plaster ready for use. The spreading of the cerate is done in the manner already outlined for regular plaster-masses, except that heat is unnecessary, since the cerate is sufficiently soft to permit of being spread by simple pressure of a spatula; in cold weather the spatula may be slightly warmed with advantage. The amount of blistering cerate necessary for a given space should not exceed 10 or 12 grains for each square inch, or about 0.120 Gm. for each square centimeter. As fly-plasters are not intended for prolonged application, ordinary muslin or adhesive plaster will answer on which to spread the cerate, the latter material being preferable on account of the adhesive edges, which serve to keep the plaster from slipping. A piece of tarletan, a trifle larger than the surface of the cerate, should be firmly pressed over the same, which, while not interfering with the blistering action of the cantharides, protects the skin from being much soiled, and prevents any of the cerate from getting under the skin if the blistered surface should be lacerated by sudden removal of the plaster.

Porous plasters, which have become very popular, differ from ordinary spread plasters in having numerous small holes punched through them, rendering them more comfortable for prolonged application, by allowing exhalations of the skin to pass off freely. They are prepared on an extensive scale by special machinery.

European dermatologists some years ago introduced a class of preparations known as *plaster-mulls*, which are intermediate in consistence between plasters and cerates. These plaster-mulls, sometimes also called salve-mulls, are especially indicated in cases in which prolonged application is necessary, since, owing to the porous character of the mull or gauze employed, they permit ready evaporation, and thus prevent maceration of the epidermis, which is likely to occur in the case of more occlusive dressings. They are sometimes prescribed as steatins and spread ointments; thus, *steatinum zinci salicylatum*, *unguentum hydrargyri extensum*, etc. The vehicle for these plaster-mulls is usually a mixture of suet and lard, containing 70 to 90 per cent. of the former, which is easily spread when heated, but does not melt nor run when applied to the body. The general mode of preparation is about as follows: A piece of mull or gauze is spread on a piece of parchment paper which has been previously moistened and pressed; the medicated mass, having been melted, is spread over the gauze by means of a broad brush when upon the point of congealing. The surface is afterward made smooth with a spatula dipped in warm water, and after having lain in a cool place for a few hours the parchment paper is removed.

The Pharmacopœia still recognizes 6 plaster-masses and 1 spread plaster, very few of which, however, are used by physicians at the present day, except official adhesive plaster for surgical purposes, and possibly belladonna plaster for its anodyne effect. The official directions for preparing the various plasters are explicit, requiring little or no additional remarks; with care and observance of the precautions before stated, good results will be obtained.

Lead plaster is, strictly speaking, a chemical compound—lead oleate or lead soap—the manufacture of which will be more fully explained in connection with the subject of saponification. It enters either directly or indirectly into the composition of all of the official plasters.

The following is a list of the Pharmacopœial plasters, showing their composition:

Plaster-Masses.

Latin Name.	English Name.	Composition.	
Emplastrum Adhæsivum	Adhesive Plaster	Rubber	20 Gm.
		Petrolatum	20 "
		Lead Plaster	960 "
Emplastrum Belladonnæ	Belladonna Plaster	Ext't of Belladonna Leaves	300 Gm.
		Adhesive Plaster	700 "
Emplastrum Hydrargyri	Mercurial Plaster	Mercury	30 Gm.
		Oleate of Mercury	1 "
		Hydrous Wool Fat	10 "
		Lead Plaster	59 "
Emplastrum Opii	Opium Plaster	Extract of Opium	6 Gm.
		Water	8 Cc.
		Adhesive Plaster	90 Gm.
Emplastrum Plumbi	Lead Plaster (Diachylon Plaster)	Lead Oleate.	
Emplastrum Saponis	Soap Plaster	Soap, dried	10 Gm.
		Lead Plaster	90 "
		Water a sufficient quantity.	

Spread Plasters.

Latin Name.	English Name.	Composition.
Emplastrum Capsici	Capsicum Plaster	Adhesive Plaster. Oleoresin of Capsicum.

SPECIAL REMARKS.

Emplastrum Adhæsivum.—The present adhesive plaster of the Pharmacopœia differs materially from the former rosin plaster which it is designed to replace. The rosin and yellow wax have been replaced by rubber and petrolatum, the former being melted at a temperature not exceeding 150° C. (302° F.) and mixed with an equal weight of petrolatum which dissolves it; to this solution lead plaster is added and the heat continued until a uniform liquid results, which is then allowed to cool.

Emplastrum Belladonnæ.—While the preparation of belladonna plaster presents no difficulty, it is essential that the extract of belladonna used be of full official strength, since the Pharmacopœia requires that the plaster, when assayed by the official method, shall yield not less than 0.38 nor more than 0.42 per cent. of mydriatic alkaloids. The Pharmacopœia also demands that all machine-spread belladonna plasters shall conform to the above standard of alkaloidal strength when tested by the official method of assay. In view of the variability in quality of the commercial belladonna plasters, the official requirement appears very desirable.

Emplastrum Capsici.—Capsicum plaster is the only plaster officially directed to be spread. The body of the plaster consists of the official adhesive plaster spread on fabric, the surface being brushed over with oleoresin of capsicum, 0.25 Gm. of the latter being contained in every space 15 centimeters square, or about $\frac{1}{10}$ grain in every square inch.

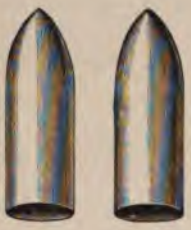
Emplastrum Opii.—Opium plaster, when made with standardized extract of opium, as it should be, contains 1.2 per cent. of morphine. A pilular extract of the proper strength is better suited for this plaster than the official powdered extract, since the latter cannot easily be reduced to the condition of a smooth paste with water; if the water be warmed, the results are more satisfactory.

Emplastrum Plumbi.—In the preparation of the official lead plaster, mutual decomposition is effected between warm solutions of 60 Gm. of lead acetate and 100 Gm. of dried Castile soap, resulting in the formation of lead oleate (mixed with a small proportion of lead palmitate, since the soap used is not pure sodium oleate), which is precipitated, and sodium acetate, which remains in solution, and is removed by washing the precipitate with hot water. The plaster is finally freed from water by kneading on a warm slab, and then wrapped in paraffin paper to protect it against the action of the air.

SUPPOSITORIES.

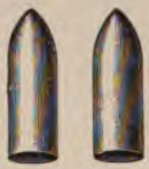
Suppositories are solid, medicinal preparations designed to be introduced into the rectum, vagina, urethra, or nose; when intended for the two last named they are usually termed bougies. They are of such consistence that, while retaining their shape at ordinary temperatures, they will slowly melt at that of the body or liquefy in the presence of moisture. The usual shape of rectal suppositories is that of a cone with a rounded apex (see Figs. 269 and 270), but the difficulty of readily introducing these into the rectum, on account of the resistance offered by contraction of the sphincter muscle, led to the suggestion of a new shape by H. S. Wellcome, of London (1893), as shown in Fig. 271, the great advantages of which become apparent when it is remembered that the bulbous end is inserted into the rectum first, and that as soon as the greatest diameter, which is about one-half inch from the point, has been passed, expulsion of the suppository is impossible, by reason of the very contractile force of the sphincter, which renders retention of the ordinary conical shape often so difficult.

Fig. 269.



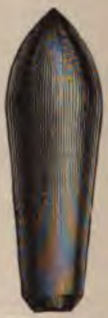
Rectal suppositories (for adults).

Fig. 270.



Rectal suppositories (for children).

Fig. 271.



The Wellcome-shape suppository.

Vaginal suppositories are made either globular or similar to rectal suppositories, as shown in Figs. 272, 273, and 274, while, for urethral and nasal bougies the pencil-shape, seen in Figs. 275, 276, and 277, has been adopted, the last-named being about one-third as long, but twice as thick as the urethral bougies.

FIG. 272.

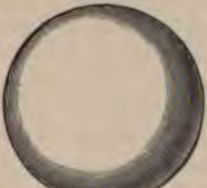


FIG. 273.

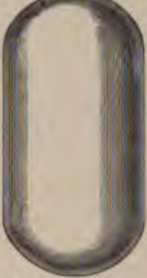
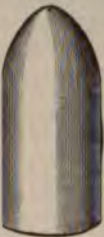
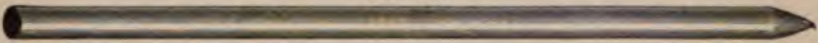


FIG. 274.



Vaginal suppositories.

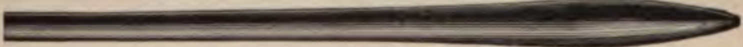
FIG. 275.



Urethral bougie.

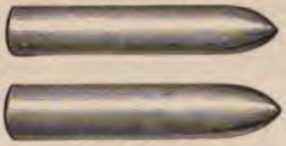
Suppositories are intended to insure a slow and uniform diffusion of their medicinal constituents to those internal parts to which they may be applied, and the choice of vehicle is made accordingly. The best substance for the preparation of suppositories is undoubtedly cacao butter, or oil of theobroma, first suggested in 1850 by the late A. B. Taylor, on account of its low fusing-point and bland, non-irritating properties. When medicinal agents, such as volatile oils, and the like, which have a softening effect on the fatty vehicle, are ordered in suppositories, and likewise during the summer season and in warm countries, it will frequently be found impossible to

FIG. 276.



The Wellcome-shape urethal bougie.

FIG. 277.



Nasal bougies.

make suppositories with a cacao butter basis without the addition of wax, which latter may be used to the extent of 5, 10, or even 20 per cent. of the weight of the fat. At the same time it must be borne in mind that the presence of a considerable quantity of insoluble matter, vegetable or mineral powders, has the tendency to raise the melting-point of the fat; in some instances the difference has been observed to be as much as 5 or 6 degrees C. (9 to 14.4 degrees F.). A mixture of glycerin and gelatin, known as glycerin jelly, is also frequently employed for vaginal suppositories and nasal and urethral bougies, on account of its ready miscibility with water. It is admirably adapted for the exhibition of solid extracts, as those of opium, belladonna, and ergot, and such substances as boric acid, hydrated chloral, iodine, iodoform, alkali bromides and iodides, ichthyol, etc. Tannic acid and alum, considered incompatible with gelatin, can nevertheless be made into satisfactory suppositories or bougies with glycerin jelly by the modified process given below. The proportions best adapted for general purposes are gelatin 20 parts, glycerin 40 parts, and water 80 parts, the whole to be reduced by evaporation to 100 parts. For some purposes these proportions may have to be changed; thus, for hygroscopic drugs, such as potassium or sodium iodide and bromide, hydrated chloral, etc., a mixture of gelatin 10 parts, water 40 parts, and glycerin 15 parts, evaporated to 25 parts, will be found much better. For vaginal suppositories and urethral bougies intended to be medicated with zinc sulphate, cupric sulphate, silver nitrate, extract of opium, corrosive mercuric chloride, etc., a mixture of gelatin 10 parts, glycerin 30 parts, and water 40 parts, evaporated to 60 parts, will be found more desirable; while for bougies and suppositories of all kinds, containing large proportions of powdered drugs insoluble in water or alcohol, a softer mass, composed of gelatin 30 parts, glycerin 15 parts, and water 120 parts, evaporated to 104 parts, is to be preferred. Glycerin jelly is prepared by soaking the gelatin in the water for a few hours, or over night, in a covered dish, then adding the glycerin and evaporating on a water-bath to the required weight.

Suppositories and bougies of alum or tannic acid with glycerin-jelly are best made with a weak solution of gelatin as follows: macerate 5 parts of gelatin with 35 parts of water, add 10 parts of glycerin, heat on a water-bath until solution is effected, and evaporate to 40 parts. To the warm mass add a hot solution of 8 parts of alum in 25 parts of water. This addition causes the gelatin to coagulate, but, on continuing the heating of the mass, it again becomes liquid. Finally, evaporate the whole to 40 parts and pour into chilled moulds. For tannin bougies, proceed exactly as in the case of alum bougies, using 1 part of tannic acid dissolved in 5 parts of glycerin in place of the hot alum solution.

The official glycerinated gelatin (Gelatinum Glycerinatum, U.S.P.) is prepared by pouring sufficient sterilized water over 100 Gm. of gelatin to cover the same, and allowing to stand for 1 hour; the water is poured off and the gelatin allowed to drain for a few minutes and transferred to a tared dish. After the addition of 100 Gm. of glycerin the mixture is heated on a water-bath until the gelatin is dissolved; the solution, while hot, is strained and the heat continued until the product weighs 200 Gm. It is too firm for use by itself as a vehicle for suppositories, and hence the Pharmacopœia directs that the medicinal agent shall be mixed with a little water and sufficient glycerin to make the weight of the mixture one-half that of the proposed finished mass, after which it is thoroughly incorporated with an equal weight of glycerinated gelatin previously melted on a water-bath.

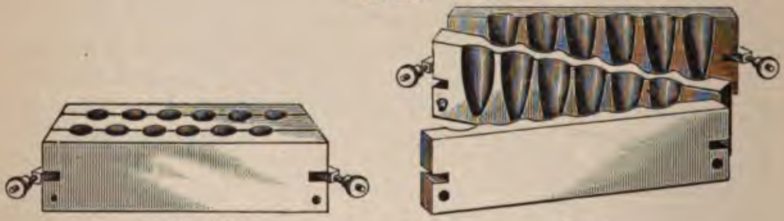
The Pharmacopœia recommends that rectal suppositories made with cacao butter should weigh about 2 Gm. (30 grains). Urethral bougies should be either 7 or 14 centimeters (2.8 or 5.6 inches) in length and weigh about 2 or 4 Gm. (30 or 60 grains) if made with glycerinated gelatin; if made with cacao butter, they should weigh about one-half as much. Vaginal suppositories should weigh about 4 Gm. (60 grains) if made with cacao butter, or 10 Gm. (150 grains) if made with glycerinated gelatin.

Since suppositories are, like ointments, simply mechanical admixtures of the medicinal constituents and a vehicle, the former must always be incorporated in the form of an impalpable powder or in a state of solution, solid extracts being rubbed into a smooth paste with water. On account of the peculiar application of suppositories, it is important that no coarse or gritty particles should ever be contained therein. They are made either entirely by hand, by casting in appropriate moulds, or by cold compression in suitable apparatus.

Hand-made suppositories are, as a rule, not so exact and uniform in shape as those moulded, although some pharmacists have attained considerable perfection and dexterity in following this convenient method. The usual plan is to effect an intimate mixture of the active ingredients and vehicle in a mortar, by forming them into a uniform mass, and transfer the mass to a graduated tile to be divided into the required number of equal parts, which are then properly shaped with the fingers. To prevent adhesion of the mass to the tile or fingers, it may be dusted with finely powdered starch or a mixture of starch and lycopodium. The method, of course, excludes the use of glycerin jelly, and, if the mass shows a disposition to crumble, the addition of a few drops of castor oil will overcome the difficulty, rendering the mass plastic. One of the best vehicles for making suppositories by hand, or by cold compression, is a mixture of cacao butter 5 parts, castor oil 1 part, and yellow wax 1 part, which fuses at about the same temperature as cacao-butter; another mixture melting at body temperature is composed of cacao butter 2 parts, hydrous wool fat and white wax, of each 1 part.

For casting suppositories in moulds it is necessary to have the mass in a fluid state. If carefully and skilfully followed, this method yields the most perfectly shaped and finished suppositories that can be made; but it requires practice to insure success, presenting more difficulties than any other method. If the fluid mass be poured into the moulds too warm, immediate separation of the insoluble ingredients occurs, which settle in the apex of the cone. If allowed to cool too fast, it will not flow properly, and fill the moulds imperfectly; the proper condition of the mass is reached when the fluid is of a thin, syrupy consistence and a slight film begins to form on the surface. High heat should be avoided in preparing the mass, a low water-bath heat being amply sufficient for melting the cacao butter or glycerin jelly. Any solid extract to be added should be softened on a slab or pill-tile with a little water, mixed with about one-third of the melted vehicle, and transferred to the dish or capsule containing the remainder of the melted vehicle, which has been removed from the water-bath and allowed to cool somewhat. By stirring with a glass rod or narrow steel spatula the extract will become uniformly incorporated, after which any solid ingredient, in impalpable powder, may be added and thoroughly mixed; the fluid mass is then immediately poured into well-chilled moulds, with constant stirring to prevent separation. It is important that no heat be applied to the melted mass after the addition of the medicinal constituents lest separation occur, particularly in the case of extracts, which cannot afterward be successfully overcome. If perchance the mixture solidifies before it is transferred to the moulds, it may again be liquefied by holding the dish or capsule over the steam arising from a hot water-bath and stirring assiduously. The moulds must be perfectly clean and dry, having been previously well chilled by placing them on ice; there will then be no occasion whatever for dusting them with lycopodium or other substance. If the fluid mass is of the right consistence and the mould cold, it will immediately congeal and contract on being poured into the moulds, but sufficient time should be allowed for the suppository to harden throughout, otherwise trouble may be experienced in removing them; in winter twenty or thirty minutes will suffice, whereas forty minutes or longer may be necessary in summer, unless the mould, after having

FIG. 278.

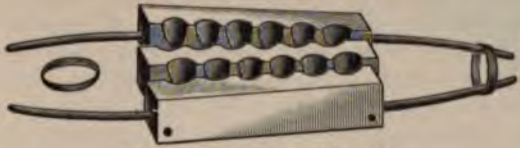


Closed. Open.

Maris' suppository mould.

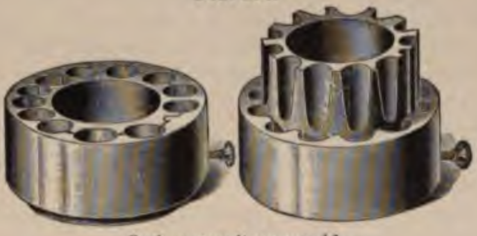
been filled, be placed in an ice-chest. Various styles of moulds are in use among pharmacists, those known as divided moulds, opening either horizontally or vertically, being preferred on account of the convenience with which they can be taken apart and cleaned. Figs. 278, 279, 280, and 281 respresent four different styles of moulds, from all of which the suppositories can be quickly removed by bearing slightly with the finger against the conical ends after the moulds have been opened.

FIG. 279.



Wirz's suppository mould (open).

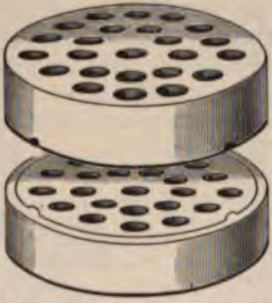
FIG. 280.



See's suppository mould.

The following medicated suppositories have at times proved troublesome, probably for want of proper understanding of the conditions present.

FIG. 281.



Blackman's suppository mould.

Suppositories of trional or **trional** and **codeine** are extensively used in some localities, especially in hospitals. Trional is soluble in hot cacao butter, but upon cooling the solution rapidly solidifies into an unmanageable mass. The best plan of incorporating the trional is to rub it up into an impalpable powder, mix it with castor oil into a smooth paste, 5 minims of oil for 20 grains of trional, and then add this to the melted cacao butter, previously cooled to about 43° C. (109.4° F.); the mixture is well stirred and poured into moulds. If codeine is to be used together with trional, it may be dissolved directly in the melted fat; but as solution takes place slowly, it is better to dissolve the alkaloid in a little alcohol and add the solution to the warm fat, when the alcohol will be dissipated; the trional is added in the manner directed above.

Suppositories of Hydrated Chloral.—If these are to be made with glycerin jelly, little or no difficulty is experienced, nor with cacao butter if the proportion of hydrated chloral is small (10 or 15 per cent.). Hydrated chloral will liquefy cacao butter if added in large quantity, and yet with the aid of a little castor oil, 5 minims for 15 grains of powdered hydrated chloral, a paste is obtained which, according to H. B. Dunning, when mixed with 15 grains of melted and cooled cacao butter, produces firm and satisfactory suppositories, containing 50 per cent. of the medicinal agent. Such suppositories should always be kept in a cool place during warm weather. P. MacEwan recommends in *Art of Dispensing* the following plan for suppositories containing 60 per cent. of hydrated chloral: Melt 60 grains of white wax (shredded) in a wide-mouth vial on a water-bath, add 180 grains of powdered hydrated chloral, shake well, and add 60 grains of cacao butter previously melted. Continue to shake until creamy and pour into chilled moulds.

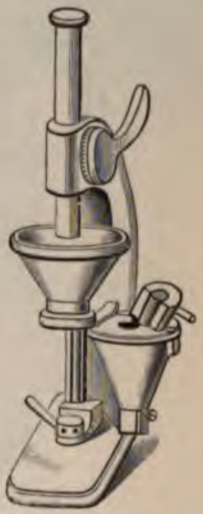
Suppositories of Tannic Acid and Extract of Belladonna.—Tannic acid, powdered nutgall, and similar astringent substances are likely to cause trouble with extract of belladonna or other alkaloidal drugs, and even without such extracts will cake if the cacao butter has a temperature above 54° C. (129.2° F.). The cold-compression method is to be preferred for all such combinations. If the suppositories are to be cast in moulds, the proper plan is to soften the extract with the smallest possible amount of water and mix it with about one-third of the melted cacao butter at a temperature between 38° and 43° C. (100.4° and 109.4° F.), using another third of the melted fat for incorporation of the finely powdered astringent. Finally, add both mixtures to the remaining fat, mix well, and pour at once into well-chilled moulds.

Suppositories of Iodoform.—Iodoform should never be mixed with melted cacao butter while the latter is hot; and if balsam of Peru is also to form part of the suppositories, it should be mixed into a smooth paste with the iodoform, which is then incorporated with about one-half of the melted cacao butter containing 10 per cent. of wax, and when thoroughly mixed, transferred to the dish containing the remainder of the fatty base, well stirred and poured into moulds.

The numerous difficulties attending the casting process have led many pharmacists to abandon this process in favor of cold compression. The chief advantages of the compression method are the saving of time and the absence of all danger of overheating and of separation of extracts and other ingredients, while the suppositories are uniform in composition and leave nothing to desire in appearance, although the finish is possibly not quite so perfect as in carefully cast suppositories. The mass for compression is prepared in a mortar, as for hand-made suppositories, and, when a uniform mixture has been obtained, it is removed and cut up into small pieces, which are placed in a hopper or barrel of the compressor.

The first successful compression mould for dispensing purposes was that known as the Archibald mould (see Fig. 282), which is still used by many. The only objection to this mould is the tedious removal of the finished suppository; the adhesion of the mass to the sides can be readily overcome, however, by swabbing the mould with a pledget of cotton dampened with glycerin between every two compressions.

Fig. 282.

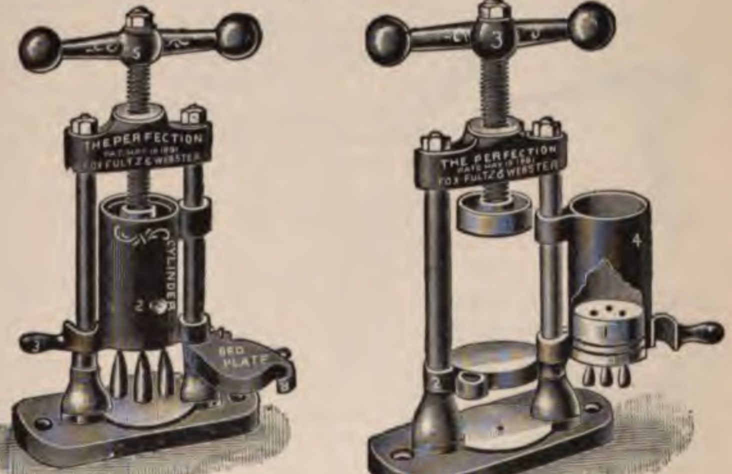


The Archibald suppository machine.

The three apparatus shown in Figs. 283, 284, and 285 are improvements on the Archibald mould in so far that 3 rectal suppositories can be compressed at once, while the finished product is easily and quickly removed. They differ from each other only in the position of the compressor, two being perpendicular and the other horizon-

Fig. 283.

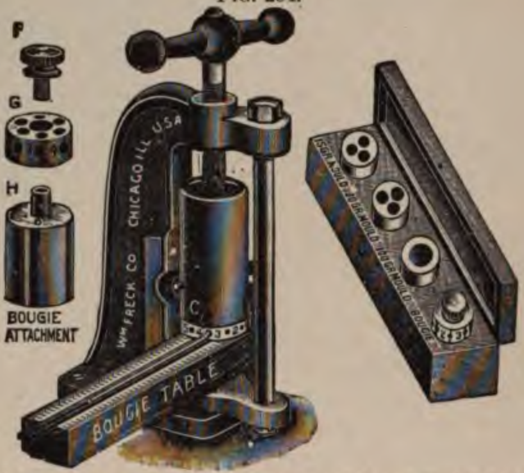
a, closed. *b*, opened.



The "Perfection" suppository machine.

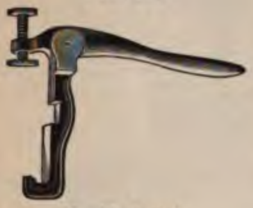
tal; all, however, require considerable effort to force the mass through the small openings in the top of the moulds into the moulds proper underneath, which is the only objection that can be urged against them. It sometimes happens that the mould becomes "fixed" in the cylinder of the "Perfection," Freck, and other suppository compressing machines, in which case it can easily be loosened by means of the device shown in Fig. 285, and known as a mould starter. Each of the 4 compression machines is provided with a set of 3 suppository moulds (2 rectal, 30 and 15 grains, and 1 vaginal) and 1 bougie mould. In the Archibald machine the moulds are placed in a swinging bed, which is secured under the cylinder by means of a lever, and after the suppository has been compressed the swinging bed is loosened, the mould taken out and opened, and the suppository removed by gently pushing it with the thumb. In the 3 other machines the moulds are screwed into the lower part of the cylinder, or slipped into the cylinder from the top, and rest firmly against an iron bed-plate; to remove the compressed suppository it is only necessary to open the bed-plate, as shown in Fig. 283, *a*, and, by one or two turns of the screw, push the suppositories out of the moulds. For the compression of nasal or urethral bougies a plate is put into the cylinder and a tube attached, through which the mass can be forced to any desired length.[1]

FIG. 284.


F
G
H
BOUGIE ATTACHMENT
Wm FRECK CO CHICAGO ILL USA
C
BOUGIE TABLE
15 GR. MOULD · 30 GR. MOULD · 100 GR. MOULD · BOUGIE

Freck's suppository machine with bougie attachment, graduated bougie table, mould box, and pipe attachment.

FIG. 285.



Mould starter.

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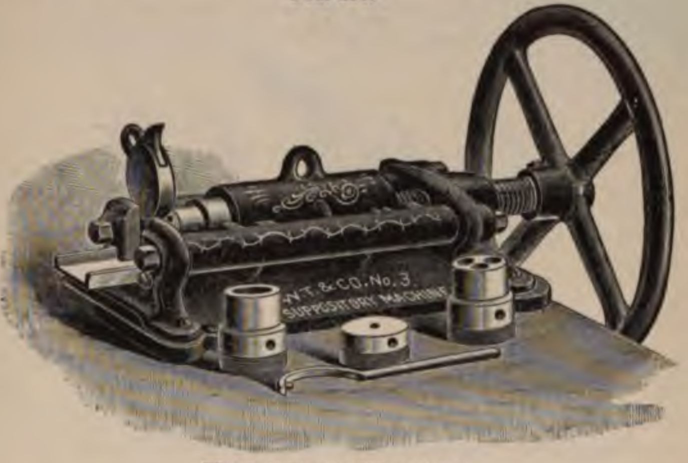
[1] The Genese suppository machine and compressor, which were illustrated and described on pages 396, 397, and 399, of the first edition, are no longer on the market, the patents and rights to manufacture the machines and suppositories having been sold to Burroughs, Wellcome & Co., of London, England.

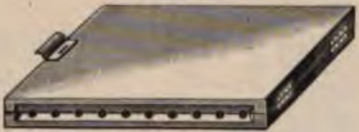
Bougies, made with glycerin jelly, are cast in special moulds, such as are shown in Figs. 287 and 288; the tubes are usually swabbed with a woollen rag carrying some liquid petroleum or olive oil, to prevent adhesion of the material. When made with cacao-butter or soap and starch they can either be compressed or formed by hand. Nasal bougies should be about 38 millimeters ($1\frac{1}{2}$ inches) in length and 6 millimeters ($\frac{1}{4}$ inch) in diameter, while urethral bougies are usually made 100 millimeters (4 inches) in length and from 3 to 4 millimeters ($\frac{1}{8}$ to $\frac{1}{6}$ inch) in diameter. The ends of both are somewhat pointed, as shown in Fig. 289.

FIG. 286.



Whitall's suppository machine.

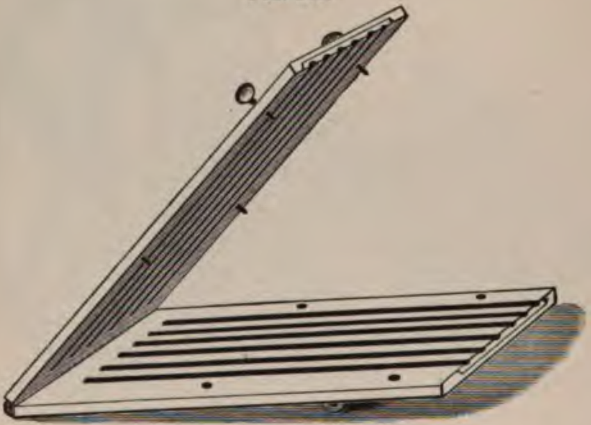
FIG. 287.



Mould for gelatin bougies.

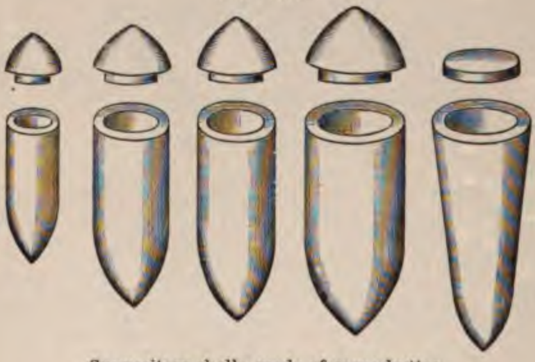
The Pharmacopœia recognizes only one special kind of suppositories, viz., those of glycerin, and gives general directions for the preparation of all others. The official glycerin suppositories are composed of 93 per cent. of glycerin and 7 per cent. of sodium stearate, and if all water has been expelled will weigh about 3.215 Gm. (50 grains) each. They are made by dissolving 0.5 Gm. of monohydrated sodium carbonate in 5 Cc. of water on a water-bath, adding first 30 Gm. of glycerin and then 2 Gm. of stearic acid, and finally heating carefully until carbon dioxide ceases to be evolved and a clear liquid results, which is then poured into a mould arranged for 10 suppositories and allowed to congeal. Since each molecule of stearic acid is capable of forming one molecule of sodium stearate, as shown by the equation $2HC_{18}H_{35}O_2 + (Na_2CO_3 + H_2O) = 2NaC_{18}H_{35}O_2 + CO_2 + 2H_2O$, 2 Gm. of the acid will form 2.155 + Gm. of sodium stearate, which is sufficient to form a solid mass with 30 Gm. of glycerin, the water and carbon dioxide being dissipated. Owing to the very hygroscopic nature of glycerin, the suppositories must either be wrapped in tinfoil or dispensed in small straight vials without a lip; some manufacturers coat them by dipping them into melted paraffin, which protects them against the air, but has the disadvantage of possibly failing to be removed by the patient before insertion, in which event the suppository would fail to act, as the heat of the body is not sufficient to melt paraffin.

FIG. 288.



Mitchell's urethral bougie mould.

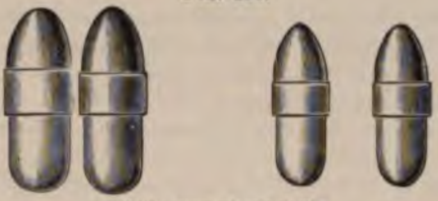
FIG. 289.



Suppository shells, made of cacao-butter.

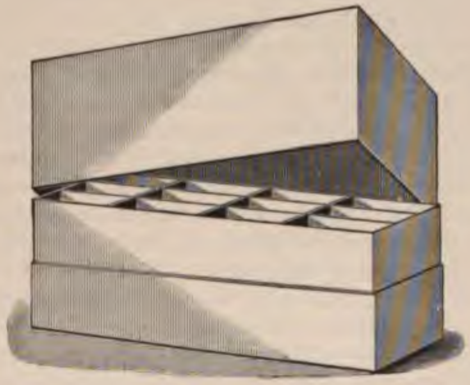
Suppository shells made of gelatin or butter of cacao have been introduced for the convenience of the dispenser, but are not used to any extent. The medicinal ingredient is intended to become mixed with the material of the shells as the latter melts, but, as this is uncertain, they should never be used in case of potent remedies or if the direct application of the active agent is likely to cause irritation; for the introduction of boric acid, iodoform, or aristol they are, however, suitable. In the case of butter of cacao shells (see Fig. 289) they are preferably filled with a mixture of the active ingredient and grated butter of cacao, and the top sealed either with a warm spatula or a little stiff mucilage of acacia. The gelatin shells (see Fig. 290) may be conveniently sealed by moistening the margin of the lower half with a little water before slipping the upper part over the same. The best method of dispensing suppositories is undoubtedly in partitioned paper boxes (see Fig. 291), the sides and bottom of which should be lined with tinfoil or paraffin paper, the patient always being directed to keep the box in a cool place; in the absence of partitioned boxes, an oblong powder-box may be used, the suppositories being placed between two pieces of sheet-wadding.

Fig. 290.



Gelatin suppository shells.

Fig. 291.



Suppository box.

CHAPTER XXXVI.

THE PRESCRIPTION.

Although the many and varied operations of the dispensing counter have been treated in the preceding chapters, a short discussion of the prescription itself seems desirable for the purpose of rendering the general information more complete.

The word *prescription* (Latin *præscriptio*, from *præ*, before, and *scribere*, to write) is defined as meaning a written order or direction to the pharmacist or druggist for compounding and dispensing a medicine. A prescription consists of several parts, namely, the superscription, the inscription, the subscription, and the signature, to which is almost always added the name or initial of the physician ordering the medicine, and frequently also the name of the patient. The following prescription written out in full may serve as a type to illustrate the various parts :

(Superscription)	Recipe.	
	Bismuthi Subnitratis,	ʒj ;
(Inscription)	Tincturæ Opii Camphoratæ,	ʒij ;
	Misturæ Cretæ, q. s. ad	℥ ij.
(Subscription)	Misce.	
(Signature)	Signa : A teaspoonful every 2 hours.	

G. W. Smith, M. D.

For Mrs. Jenkins' infant.

The first three parts of a prescription are written, with rare exception, in the Latin language, because it is the language of science and not subject to change like modern languages. Free use is made of abbreviations, which are readily understood by pharmacists the world over. The superscription consists of a single character, R, the initial letter of the Latin word *recipe*, meaning take thou ; in France the letter P is used, the initial letter of the word *prenez*. In olden times the character ♃ was usually placed at the head of prescriptions and formulas ; this was the sign of Jupiter, the chief deity of the ancient Romans, and was probably intended as an invocation to the gods ; a portion of this character is still used by some physicians in conjunction with the letter R, thus ℞, merely as an ornamentation and probably without any knowledge of its origin.

The inscription is the most important part of the prescription, since it contains the names and quantities of the ingredients of the medicine ordered. The names of the medicines are written in abbreviated form, and the quantities are always indicated by symbols, gr., ℈, ʒ, ℥, and Roman numerals, except in the case of metric prescriptions. In the latter case the quantities are always designated by Arabic numerals, properly divided by the decimal point, and frequently followed by the signs Gm. or Cc.; in continental Europe the signs Gm. and Cc. are rarely employed, because Gm. is always understood, all substances, liquid as well as solid, being dispensed by weight. The inscription may be conveniently subdivided into several parts according to the importance of the several ingredients: thus, the *basis* or chief active agent; the *adjuvant* or agent second in importance, and intended to aid the basis; the *corrective*, intended to modify the action of the preceding agents; lastly, the *vehicle* or *diluent*, intended to provide a convenient and acceptable form of administration. It must not be supposed, however, that every inscription consists of four subdivisions, for sometimes only the basis and vehicle, or even the basis alone, may be prescribed.

The subscription is intended to give directions to the compounder as to the manner in which the medicine is to be dispensed, whether in divided doses or as a whole. These directions are more or less incomplete, consisting sometimes of a single letter, as *M.* for *misce*, *F.* for *fiat;* or *S.* for *solve*, or a combination of abbreviations, as *Ft. mist.* for *fiat mistura*, *Ft. pulv.* for *fiat pulvis*, *Ft. sol.* for *fiat solutio*, etc. Frequently the subscription is so incomplete as to be without meaning unless the missing portion is mentally supplied, as, for instance, *Ft. chart. x*, so often written when the physician desires the medicine to be divided into 10 powders; literally translated, this subscription would read, *10 papers may be made* (*fiant chartæ decem*). The missing portion to be supplied may be *p. et div. in*, and if added to the above abbreviation causes the same to read, *fiat pulvis et divide in chartas x*, or *let a powder be made and divide into 10 papers.* In order to be able to read physicians' prescriptions intelligently and to write the abbreviated names and terms out in full when desired, it is necessary to be familiar with the numerous Latin titles of medicines and the many words used in the subscription. For convenience of study and reference, a table of abbreviations likely to occur in prescriptions is given on page 457.

The signature, or directions as to how the medicine is to be taken, is always written in English in this country, while in Great Britain the Latin language is still occasionally used. It is important that the signature be written in a clear, legible hand, so that neither dispenser nor patient be left in doubt as to the dose intended, and it is very unfortunate that some physicians will persist in giving verbal directions to their patients and marking their prescriptions simply *use as directed*, which may lead to much confusion.

The following prescriptions are given for the purpose of acquainting the student with the use of various abbreviations common in prescription-writing, and which, by a careful comparison of the abbreviated and unabbreviated forms and subsequent reference to the translation, will enable him to become familiar with this part of the work of the dispensing-counter.

Abbreviated Form.	Unabbreviated Form.	Translation.
℞	Recipe	Take
Quin. Sulph. . . . . . gr. xxiv.	Quininæ Sulphatis grana viginiti quatuor.	Of Sulphate of Quinine . . 24 grains.
Ferr. Sulph. . . . . . gr. vj.	Ferri Sulphatis grana sex.	Of Sulphate of Iron . . . 6 grains.
Magn. Sulph. . . . . . ʒij.	Magnesii Sulphatis drachmas duas.	Of Sulphate of Magnesium 2 drachms.
Acid. Sulph. Ar. . . . q. s.	Acidi Sulphurici Aromatici quantum sufficiat.	Of Aromatic Sulphuric Acid so much as may suffice.
Syr. Aurant. . . . . . ℥j.	Syrupi Aurantii unciam unam.	Of Syrup of Orange . . . . 1 ounce.
Aq. Dest. . . . . . . ℥v.	Aquæ Destillatæ uncias quinque.	Of Distilled Water . . . . 5 ounces.
Ft. sol.	Fiat solutio.	Let a solution be made.
℞	Recipe	Take
Ext. Bellad. Fol. . . . gr. xxx.	Extracti Belladonnæ Foliorum grana triginta.	Of Extract of Leaves of Belladonna . . . . 30 grains.
Camph. Trit. . . . . . ℈ij.	Camphoræ Tritæ scrupulos duos.	Of Ground Camphor . . . 2 scruples.
P. Gallæ . . . . ʒj.	Pulveris Gallæ drachmam unam.	Of Powdered Nutgall . . . 1 drachm.
Adip. Benz. . . . . . ℥j.	Adipis Benzoinati unciam unam.	Of Benzoinated Lard . . . 1 ounce.
M. ft. ungt. d. ad oll.	Misce; fiat unguentum, detur ad ollam.	Mix; let an ointment be made; let it be put into a jar.
℞	Recipe	Take
Bism. Subcarb.	Bismuthi Subcarbonatis	Of Bismuth Subcarbonate
Sod. Bicarb. . . . āā ʒij.	Sodii Bicarbonatis ana drachmas duas.	Of Sodium Bicarbonate of each 2 drachms.
Tinct. Nuc. Vom. . . . ʒj.	Tincturæ Nucis Vomicæ drachmam unam.	Of Tincture of Nux Vomica 1 drachm.
Glycerin. . . . . . . ℥ss.	Glycerini unciam unam.	Of Glycerin . . . . 1 ounce.
Aq. Menth. Pip. q. s. ad ℥iv.	Aquæ Menthæ Piperitæ quantum sufficiat ad uncias quatuor.	Of Water of Peppermint . so much as may suffice to (make the volume) 4 ounces.
Ft. mist.	Fiat mistura.	Let a mixture be made.
℞	Recipe	Take
P. Opii . . . . gr. v.	Pulveris Opii grana quinque.	Of Powder of Opium . . . 5 grains.
Camph. . . . . gr. x.	Camphoræ grana decem.	Of Camphor . . . . 10 grains.
Sacch. Alb. . . . . . . gr. xv.	Sacchari Albi grana quindecim.	Of White Sugar . . . . . . 15 grains.
M. ft. p. div. in p. æq. No. x; disp. in ch. cer.	Misce; fiat pulvis; divide in partes æquales numero decem; dispensentur in charta ceratâ.	Mix; let a powder be made· divide into equal parts 10 in number; let them be dispensed in waxed paper.

Abbreviated Form.		Unabbreviated Form.		Translation.	
℞		Recipe		Take	
Hyd. Chlor. Mit. . . .	gr. ij.	Hydrargyri Chloridi Mitis	grana duo.	Of Mild Chloride of Mercury	2 grains.
Sacch. Alb.	℈j.	Sacchari Albi	scrupulum unum.	Of White Sugar	1 scruple.
M. ft. p. in ch. xij div.		Misce; fiat pulvis in chartas duodecim dividendus.		Mix; let a powder be made to be divided into 12 papers.	
℞		Recipe		Take	
Zinc. Oxid. Opt. . . .	ʒij.	Zinci Oxidi, optimi	drachmas duas.	Of Oxide of Zinc, best . . .	2 drachms.
Sem. Lycopod.	℥ss.	Seminis Lycopodii	unciam dimidiam.	Of Seed of Lycopodium . .	½ ounce.
Ol. Rosæ	gtt. v.	Olei Rosæ	guttas quinque.	Of Oil of Rose	5 drops.
Amyl. Maid. . . q. s. ad	℥ij.	Amyli Maidis	quantum sufficiat ad uncias duas.	Of Corn Starch	so much as may suffice to (make the weight) two ounces.
M. ft. p. subt. d. ad scat.		Misce; fiat pulvis subtilissimus; detur ad scatulam.		Mix; let a very smooth powder be made; let it be put in a box.	
℞		Recipe		Take	
Ol. Tereb	ʒij.	Olei Terebinthinæ	drachmas duas.	Of Oil of Turpentine . . .	2 drachms.
Ol. Ricin.	℥j.	Olei Ricini	unciam unam.	Of Castor Oil	1 ounce.
P. Acac.	q. s.	Pulveris Acaciæ	quantum sufficiat.	Of Powder of Acacia . . .	so much as may suffice.
Syr. Tolut.	℥j.	Syrupi Tolutani	unciam unam.	Of Syrup of Tolu	1 ounce.
Aq. Cinnam.	℥ij.	Aquæ Cinnamomi	uncias duas.	Of Water of Cinnamon . .	2 ounces.
M. ft. emuls. sec. art.		Misce; fiat emulsio secundum artem.		Mix; let an emulsion be made according to art.	
℞		Recipe		Take	
Pot. Brom.	15.0 Gm.	Potassii Bromidi	grammata quindecim.	Of Bromide of Potassium .	15 grammes.
Aq. Menth. Vir. . . .	125.0 Cc.	Aquæ Menthæ Viridis	centimetra cubica centum et viginti quinque.	Of Water of Spearmint . .	125 cubic centimeters.
Ft. sol.		Fiat solutio.		Let a solution be made.	
℞		Recipe		Take	
Plumb. Acet.	1.5 Gm.	Plumbi Acetatis	gramma unum et dimidium.	Of Acetate of Lead	1½ grammes.
P. Opii	0.65 "	Pulveris Opii	centigrammata sexaginta quinque.	Of Powder of Opium . . .	65 centigrammes.
Camph.	0.50 "	Camphoræ	decigrammata quinque.	Of Camphor	5 decigrammes.
M. ft. mass. in pil. xij div.		Misce; fiat massa in pilulas duodecim dividenda.		Mix; let a mass be made to be divided into 12 pills.	

Abbreviated Form.	Unabbreviated Form.	Translation.
℞	Recipe	Take
Cocain. Hydrochl. . 0.20 Gm.	Cocainæ Hydrochloridi decigrammata duo.	Of Hydrochloride of Cocaine 2 decigrammes.
Ac. Borac. . . . . . 0.32 "	Acidi Boracici centigrammata triginta duo.	Of Boracic Acid . . . . . 32 centigrammes.
Aq. Dest. . . . . . . 10.0 Cc.	Aquæ Destillatæ centimetra cubica decem.	Of Distilled Water . . . . 10 cubic centimeters.
M. ft. collyr. filt.	Misce, fiat collyrium : filtra.	Mix; let an eyewash be made; filter.
℞	Recipe	Take
Ferr. Sulph. Cryst. . 6.0 Gm.	Ferri Sulphatis Crystallisati grammata sex.	Of Crystallized Sulphate of Iron . . . . 6 grammes.
Myrrh. Elect.	Myrrhæ electæ	Of Select Myrrh .
Sacch. Alb. . . āā 18.0 Gm.	Sacchari Albi ana grammata octodecim	Of White Sugar . of each 18 grammes.
Pot. Carb. . . . . . 8.0 "	Potassii Carbonatis grammata octo.	Of Carbonate of Potassium . 8 grammes.
Spir. Lavand. . . . 60.0 Cc.	Spiriti Lavandulæ centimetra cubica sexaginta.	Of Spirit of Lavender . . . 60 cubic centimeters.
Aq. Rosæ . q. s. ad 1000.0 "	Aquæ Rosæ quantum sufficiat ad centimetra cubica mille.	Of Rose-water . . . so much as may suffice to (make the volume) 1000 cubic centimeters.
Ft. mist.	Fiat mistura.	Let a mixture be made.
℞	Recipe	Take
Acid. Arsen. . . . . 0.002 Gm.	Acidi Arsenosi milligrammata duo.	Of Arsenous Acid . . . . 2 milligrammes.
P. Piper. Nig. . . . 0.065 "	Pulveris Piperis Nigri milligrammata sexaginta quinque.	Of Powder of Black Pepper 65 milligrammes.
M. ft. pil. d. tal. dos. No. xxx.	Misce; fiat pilula; dentur tales doses numero triginta.	Mix; let a pill be made; let such doses be given 30 in number (let 30 such doses be given).
℞	Recipe	Take
Sod. Carb. . . . . . 3.0 Gm.	Sodii Carbonatis grammata tria.	Of Carbonate of Sodium . . 3 grammes.
Acid. Stearic. . . . . 5.0 "	Acidi Stearici grammata quinque.	Of Stearic Acid . . . . . . 5 grammes.
Glycerin. . . . . . . 60.0 "	Glycerini grammata sexaginta.	Of Glycerin . . . . 60 grammes.
M. ft. mass. ex qua form. suppos. rect. No. x; dent. ad vitr. ben. claus.	Misce; fiat massa ex quâ formentur suppositoria rectalia numero decem; dentur ad vitrum bene clausum.	Mix; let a mass be made out of which may be formed rectal suppositories 10 in number; let them be put into a well-closed bottle.
℞	Recipe	Take
Sod. Salicyl. . . . . 15.0 Gm.	Sodii Salicylatis grammata quindecim.	Of Salicylate of Sodium . . 15 grammes.
D. in p. æq. No. xij; d. ad caps. amyl.	Divide in partes æquales numero duodecim; dentur ad capsulas amylaceas.	Divide into equal parts, 12 in number; let them be put into starch capsules-(wafers or cachets).

It will be observed in the above prescriptions that in every instance the ingredients are written in the genitive (possessive) case, and the quantities, whether by weight or measure, in the accusative (objective) case. This arrangement will be better understood after the analysis of the following prescription has been carefully studied.[1]

℞—Potassii Citratis . . . . ʒij (drachmas duas).
Spiriti Ætheris Nitrosi . . } ãã ʒij (ana drachmas duas).
Vini Colchici Radicis . . . }
Syrupi Acidi Citrici . . . . ℥j (unciam unam).
Aquæ Menthæ Viridis . q. s. ad ℥iv (quantum sufficiat ad uncias quatuor).
Ft. sol. (fiat solutio).

As explained on page 451, the letter *R* stands for the word *Recipe*, the imperative mood of the transitive verb *Recipio, recipere, recepi, receptum*, third conjugation, meaning to receive or to take; hence the imperative *Recipe* means "take thou," and the object of the verb, in this case the quantity of ingredient ordered, must be in the accusative (objective) case, according to the rule, that a transitive verb in the active voice governs a noun in the objective case. The word *recipe* although indicated but once, at the head of the prescription, must be understood as governing the quantity of every ingredient prescribed.

Potassii (of potassium) is the genitive singular of *potassium*, a neuter noun of the second declension, and is governed by *citratis*, according to the rule that a noun limiting the signification of another noun governs the same in the genitive (possessive) case.

Citratis (of citrate) is the genitive singular of *citras*, a feminine noun of the third declension, and is governed by *drachmas*, according to the rule that a noun denoting quantity, quality, or property governs another noun, to which it is so related, in the genitive case.

Drachmas (drachms) is the accusative plural of *drachma*, a feminine noun of the first declension, and is the object of the verb *recipe*.

Duas (two) is the accusative plural feminine of the numeral adjective *duo, duæ, duo*, and qualifies *drachmas*, with which it must agree in case, number, and gender.

Spiriti (of spirit) is the genitive singular of *spiritus*, a masculine noun of the second declension, and is governed by *drachmas*, according to the rule stated under *citratis*.

Ætheris (of ether) is the genitive singular of *æther*, a masculine noun of the third declension, and is governed by *spiriti*, according to the rule given under *potassii*.

Nitrosi (of nitrous) is the genitive singular masculine of the adjective *nitrosus, nitrosa, nitrosum*, and qualifies *ætheris*, according to the rule given under *duas*.

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[1] Students desirous of gaining further information on this subject are referred to the following books: Robinson's *Latin Grammar of Pharmacy and Medicine; The Latin Grammar of Pharmacy*, by Joseph Ince (England), and *Elements of Latin for Students of Pharmacy and Medicine*, by Crothers and Bice.

Vini (of wine) is the genitive singular of *vinum*, a neuter noun of the second declension, and is governed by *drachmas*, according to the rule given under *citratis*.

Colchici (of colchicum) is the genitive singular of *colchicum*, a neuter noun of the second declension, and is governed by *radicis*, according to the rule given under *potassii*.

Radicis (of root) is the genitive singular of *radix*, a feminine noun of the third declension, and is governed by *vini*, according to the rule given under *potassii*.

Ana (of each) is a Greek preposition governing the accusative case, and as such has a distributive effect. Although the abbreviated form *āā* is extensively employed, it would seem more correct to use instead the Latin adjective *singulorum* to indicate "of each," usually abbreviated *sing.*, and this is done by some physicians, particularly in Germany. The abbreviation *āā* or *sing.* may be used in connection with any number of ingredients and is usually written opposite the last one of the series to which it is intended to apply.

Drachmas (drachms) as above.

Duas (two) as above.

Syrupi (of syrup) is the genitive singular of *syrupus*, a masculine noun of the second declension, and is governed by *unciam*, according to the rule given under *citratis*.

Acidi (of acid) is the genitive singular of *acidum*, a neuter noun of the second declension, and is governed by *syrupi*, according to the rule given under *potassii*.

Citrici (of citric) is the genitive singular neuter of the adjective *citricus, citrica, citricum*, and qualifies *acidi*, according to the rule given under *duas*.

Unciam (ounce) is the accusative singular of *uncia*, a feminine noun of the first declension, and is the object of the verb *recipe*.

Unam (one) is the accusative singular feminine of the numeral adjective *unus, una, unum*, and qualifies *unciam*, according to the rule given under *duas*.

Aquæ (of water) is the genitive singular of *aqua*, a feminine noun of the first declension, and is governed by *tantum*, understood (see *quantum*), according to the rule given under *citratis*.

Menthæ (of mint) is the genitive singular of *mentha*, a feminine noun of the first declension, and is governed by *aquæ*, according to the rule given under *potassii*.

Viridis (of green) is the genitive singular feminine of the adjective *viridis, viridis, viride*, and qualifies *menthæ*, according to the rule given under *duas*.

Quantum (how much) may be parsed as an adverb of quantity qualifying the verb *sufficiat*, but it is better to parse it as a relative adjective with the adjective *tantum* (so much) as its redditive. In either case the adjective *tantum* is understood and governs *aquæ*, according to the rule that adjectives in the neuter gender, without a substantive, are regarded as nouns and govern the genitive case. *Tantum* is never used jointly with *quantum* in prescriptions, but the former is always understood, and the translation, whether both words are used or only the latter, is invariably "so much as."

Sufficiat (may suffice or may be sufficient), is the third person singular, subjunctive mood, present tense, of the intransitive verb *sufficio, sufficere, suffeci, suffectum*, third conjugation, meaning to suffice or to be sufficient, and is governed by *quantum* as its subject.

Ad (to) is a preposition governing the accusative *uncias*.

Uncias (ounces) is the accusative plural of *uncia*, a feminine noun of the first declension, and is governed by the preposition *ad*.

Quatuor (four) is an indeclinable numeral adjective and qualifies *uncias*.

Fiat (may be made or let there be made) is the third person singular, subjunctive mood, present tense, of the irregular verb *fio, fieri, factus*, meaning to be made or done, and has *solutio* for its subject.

Solutio (solution) is the nominative singular of *solutio*, a feminine noun of the third declension, and is the subject of the verb *fiat*.

LIST OF ABBREVIATIONS AND TERMS USED IN PRESCRIPTIONS.

Abbreviation.	Term or Phrase.	Meaning.
ā or āā	ana	of each.
Add. or Addat.	Adde or addatur	Add or let it be added.
Ad. libit.	Ad libitum	At pleasure.
Aeq.	Aequalis, is, e	Equal.
Agit. or Agitet.	Agita or agitetur	Shake or let it be shaken.
Alb.	Albus, a, um	White.
Ant.	Ante	Before.
Arom.	Aromaticus, a, um	Aromatic.
Aq.	Aqua	Water.
Aq. bull.	Aqua bulliens	Boiling water.
Aq. ferv.	Aqua fervida	Hot water.
Aq. saturn.	Aqua saturni	Lead-water.
Aq. phaged. fl.	Aqua phagedenica flava	Yellow wash.
Aq. phaged. nig.	Aqua phagedenica nigra	Black wash.
Aquil. alb.	Aquila alba	Calomel.
Argill.	Argilla	Clay.
Bacill.	Bacillum	Bougie.
Baln. aren.	Balneum arenæ	Sand-bath.
Baln. mar.	Balneum maris	Saltwater-bath.
Baln. vap.	Balneum vaporis	Steam-bath.
Ben.	Bene	Well.
B. or Bis. i. d.	Bis in die	Twice a day.
Brev.	Brevis, is, e	Short.
Bull.	Bulliat or bulliant	Let it (or them) boil.
Cærul.	Cæruleus, a, um	Blue.
Calef.	Calefactus, a, um	Warmed.
Cap.	Capiat	May be taken.
Caps.	Capsula	Capsule.
Caps. amyl.	Capsulæ amylaceæ	Cachets.
Caps. gelat.	Capsulæ gelatinosæ	Gelatin capsules.
Carbas.	Carbasus	Lint.

Abbreviation.	Term or Phrase.	Meaning.
Cœn.	Cœna or cena.	Supper.
Cer. or Cerat.	Ceratum or	Cerate
	Ceratus, a, um	Waxed.
Chart.	Charta	Paper.
Chartul.	Chartula	Small paper.
Ch. cer. or Chart. cerat.	Charta cerata	Waxed paper.
Chart. pergam.	Charta pergamentoria	Parchment paper.
Cib.	Cibus	Food.
Cito disp.	Cito dispensetur.	Let it be dispensed quickly.
Claus.	Clausus, a, um	Closed, inclosed.
Cochl.	Cochlear	Spoon.
Cochl. magn.	Cochlear magnum	A large (table) spoon.
Cochl. parv.	Cochlear parvum	A small (tea) spoon.
Cochl. mod.	Cochlear modicum	A medium (dessert) spoon.
Col. or Colet.	Cola or coletur	Strain or let it be strained.
Collun.	Collunarium	A nose-wash.
Collut.	Collutorium	A mouth-wash.
Collyr.	Collyrium	An eye-wash.
Consp.	Consperge	Dust or sprinkle.
Contus.	Contunde or contusus	Bruise or bruised.
Coq.	Coque	Boil.
Cong.	Congius	Gallon.
Comp.	Compositus, a, um	Compound.
D.	Da, detur, or dentur	Give, it (or they) may be given.
D. or dent. t. d.	Da or dentur tales doses	Give or let there be given such doses.
Det. or dent.	Detur or dentur	Let there be given.
Dec. or decoct.	Decoctum	Decoction.
De d. in d.	De die in diem	From day to day.
Dieb. alt.	Diebus alternis	Every other day.
Dig.	Digere or digeretur	Digest or it may be digested.
Disp.	Dispensetur or dispensentur	Let there be dispensed.
Div. or divid.	Divide, dividatur or	Divide or it may be divided.
	Dividendus, a, um	To be divided.
Dos.	Dosis or doses	Dose or doses.
Elect.	Electuarium	Electuary.
Emp. or Empl.	Emplastrum	Plaster.
Empl. lytt.	Emplastrum lyttæ	Blistering plaster.
Empl. epist.	Emplastrum epispasticum	Blistering plaster.
Empl. vesic.	Emplastrum vesicans or vesicatorium	Blistering plaster.
Emuls.	Emulsio	Emulsion.
Emuls. oleos.	Emulsio oleosa	Oil emulsion.
Epist. or Epistom.	Epistomium	Stopper.
Epist. elast.	Epistomium elasticum	Rubber stopper.
Epist. vitr.	Epistomium vitreum	Glass stopper.
E. m. p.	Ex modo præscripto	As directed.
Ex aq.	Ex aqua	From (with) water.
Ex qua form.	Ex qua formentur	From which there may be formed.
Extend.	Extende	Spread.
Ext. sup. cor.	Extende supra corium	Spread upon leather.
Ext. sup. alut.	Extende supra alutam	Spread upon leather.
Ext. or Extr.	Extractum	Extract.
Ext. or Extr. fl.	Extractum fluidum	Fluid extract.
F. or Ft.	Fiat or fiant	Let there be made.
F. l. a.	Fiat lege artis	Let there be made according to (by the law of) art.
F. s. a.	Fiat secundum artem	Let there be made according to art.
Ferv.	Fervidus, a, um,	Hot.

Abbreviation.	Term or Phrase.	Meaning.
Filt.	Filtra	Filter.
Flav.	Flavus, a, um	Yellow.
Fld.	Fluidus, a, um	Fluid.
Frig.	Frigidus, a, um	Cold.
Garg.	Gargarisma	Gargle.
Gm.	Gramma or grammata	Gramme or grammes.
Gtt. or Gutt.	Gutta or guttæ	Drop or drops.
Gr.	Granum or grana	Grain or grains.
Guttat.	Guttatim	By drops.
Haust.	Haustus	Draught.
Hor. somn.	Hora somnis	At bed-time.
Inf.	Infunde or infusum	Infuse or infusion.
L. a.	Lege artis	According to (by the law of) art.
Lin. or Linim.	Linimentum	Liniment.
Liq.	Liquor	Liquor or solution.
Mac. or Macer.	Macera	Macerate.
Levit.	Leviter	Lightly.
Levit. claus.	Leviter clausus, a, um	Lightly or loosely closed.
Lut.	Luteus, a, um	Golden yellow.
Mag.	Magnus, a, um	Large.
Mass.	Massa	Mass.
M. or Misc.	Misce or misceantur	Mix or let them be mixed.
M. bene	Misce bene	Mix well.
M. caute	Misce caute	Mix cautiously.
Mist.	Mistura	Mixture.
Mod.	Modicus, a, um	Moderate (sized).
Mic. pan.	Mica panis	Crumb of bread.
Mit.	Mitte or mittatur	Send or let there be sent.
Mit. tal.	Mitte or mittantur tales	Send or let there be sent such.
Nig.	Niger, nigra, nigrum	Black.
No.	Numero	By or in number.
Non-rep.	Non-repetatur	It is not to be repeated.
O.	Octarius	Pint.
Obduc.	Obduce or obducatur	Cover or let it be covered.
Obduct.	Obductus, a, um	Covered, coated.
Ol.	Oleum	Oil.
Oleos.	Oleosus, a, um	Oily, made of oil.
Oll.	Olla	Jar.
Omn. hor.	Omni hora	Every hour.
Omn. man.	Omni mane	Every morning.
Omn. noct.	Omni nocte	Every night.
Opt.	Optimus, a, um	Best.
P. or Part.	Pars or partes	Part or parts.
P. or Part. æq.	Partes æquales	Equal parts.
P. c., p. cib., or post cib.	Post cibum	After food.
P. r. n.	Pro re nata	As occasion arises; as needed; occasionally.
P. or post prand.	Post prandium	After dinner.
P. or Pulv.	Pulvis or pulveres	Powder or powders.
Par.	Para, paretur, or paratus	Prepare, let it be prepared, or prepared.
Parv.	Parvus, a, um	Small.
Pil. or Pilul.	Pilula or pilulæ	Pill or pills.
Pulv. gross.	Pulvis grossus	Coarse powder.
Pulv. subt.	Pulvis subtilissimus	Very smooth powder.
Q. l. or Q. p.	Quantum libet or Quantum placet	As much as you please.
Q. s.	Quantum satis, Quantum sufficit, or Quantum sufficiat	A sufficient quantity.

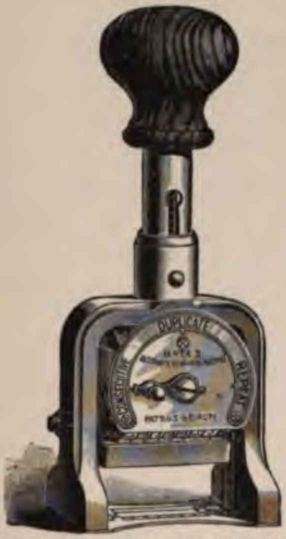
Abbreviation.	Term or Phrase.	Meaning.
R. or Recip.	Recipe	Take thou.
Rept.	Repetatur	Let it be repeated.
Rub.	Ruber, rubra, rubrum	Red.
S. a.	Secundem artem	According to art.
S. l.	Secundem legem	According to law.
S. or Solv.	Solve or solvatur	Dissolve or let it be dissolved.
Scat.	Scatula	Box.
Sem.	Semen or semina	Seed.
Sig.	Signa or signetur	Mark (label) or let it be marked (labeled).
Simp.	Simplex	Simple.
Sing.	Singulorum	Of each.
Sol. or Solut.	Solutio	Solution.
Spiss.	Spissus, a, um	Hard.
Supp. or Suppos.	Suppositorium or suppositoria	Suppository or suppositories.
Sum.	Sume or sumatur	Take or let there be taken.
Syr. or Syrup.	Syrupus	Syrup.
Tab.	Tabella or tabellæ	Tablet or tablets.
Tal.	Talis or tales	Such.
T. or ter i. d.	Ter in die	Three times a day.
Ter.	Tere	Rub or triturate.
Tinct. or. Tr.	Tinctura	Tincture.
Troch.	Trochiscus or trochisci	Lozenge or lozenges.
Ungt.	Unguentum	Ointment.
Ust.	Ustus, a, um	Burned.
Ut dict.	Ut dictum	As directed.
Vitr.	Vitreus, a, um, or vitrum	Of glass or glass.

In addition to the date usually marked on the prescription, it is customary also to place a number thereon, for the purpose of ready reference in case the prescription is to be repeated. Such numbering may be done with pen and ink, but it is preferably imprinted with a numbering machine, since the latter has the great advantage of obviating the danger of duplication of the same number on two or more prescriptions. In Fig. 292 is shown such an automatic numbering machine, which can be arranged so as to print numbers in duplicate or triplicate if desired and then changes automatically after producing each set; it can be made to print consecutive numbers, or repeat the same number indefinitely. The figures from which the machine prints are made of steel, and are freshly inked after each movement of the machine; all parts are interchangeable. The numbering capacity ranges from 1–9999 to 1–9999999, according to the number of wheels with which the machine is supplied.

For the preservation of prescriptions various devices are in use. Some pharmacists simply file the prescriptions on a heavy steel wire, claiming that, as the repetitions are few in number comparatively, this plan is convenient and less laborious than others. In some stores the prescriptions are pasted into large scrap-books, especially made for that purpose, the leaves of which are of heavy manilla paper and secured to a wood back, the binding being of stout canvas. In Fig. 293 may be seen one of the styles of prescription-books which serves the purpose admirably of preserving the original prescriptions intact. Some pharmacists prefer to put the prescriptions up carefully in bundles of one hundred or more, between thin boards, and storing them in boxes in drawers of a cabinet, appropriately marked. Lastly, a few still follow the plan, at one time much in vogue, of copying the prescriptions into a book kept for that purpose; this plan, while no doubt convenient for reference, is open to the serious objection of possible errors made in copying, and must therefore be carried out with great care.

The ownership of the prescription is still an unsettled question. While some claim that the prescription is simply an order on the pharmacist from the physician, and that therefore the former is the proper custodian of the same, there are others who insist that the prescription is but the written advice of the physician to his patient, for which the latter has paid, and to the sole ownership of which he has full legal right, as much so as a client has to the written opinion of his lawyer whom he has consulted and paid. The latter view prevails in Germany, where prescriptions are never retained by the pharmacist, but invariably handed back to the customer with the medicine, except in cases where the medicine is not paid for at the time of delivery, the prescription being held until payment is made and then returned. As a rule, the original prescription is retained by the pharmacist in this country, who, however, rarely refuses to give a copy to the customer if the same is asked for; this plan seems most desirable, as it leaves in the hands of the pharmacist the only legal evidence of what the physician has actually prescribed, in case a dispute should arise as to the correct dispensing of the medicine.

Fig. 292.



Bates' automatic numbering machine.

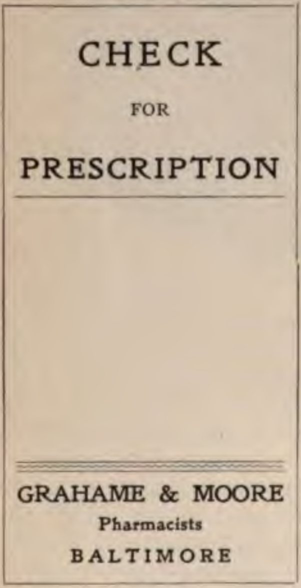
Fig. 293.

Whitall's prescription book.

The indiscriminate repetition of medicine, especially if the latter be of a potent or dangerous character, is to be strongly condemned. Serious results have been known to follow the unwarranted repeated dispensing of medicines containing cocaine hydrochloride, morphine sulphate, and similar dangerous preparations. Some physicians severely criticise the repetition of any prescription without special order, but forget that the pharmacist may have no knowledge of the physician's wishes in this respect, since a verbal order to have the medicine refilled is frequently given to the patient by the physician. The words "Not to be repeated," placed at the head of the prescription would prove an easy and effectual means of preventing repetition without the physician's order, for every respectable pharmacist would promptly and cheerfully comply with such a request. In the absence of instructions from the physician, the request for a copy of a prescription by the customer, or for repetition of any ordinary medicine, cannot well be refused, but judgment is necessary in order that the original prescription be not abused and made to do service for a number of outside persons who have no claim upon it, whereby the physician would be made to suffer financially.

In order to guard against confusion and mistakes in the compounding and delivery of medicines, a check system is in use in many stores, and is to be highly commended. The best of these is probably the following: When a prescription is handed in by a customer, it is at once numbered by the person receiving it and at the same time two checks, made of pasteboard and of the size and style shown in Fig. 294, are stamped with the same number by means of the automatic numbering machine mentioned above. One of the checks is handed to the customer and the other accompanies the prescription to the dispensing-counter, to be afterward attached to the bottle, box, or jar of medicine when completed. On this second check are also marked the price of the medicine, whether paid or not, and such other information as may appear desirable.

FIG. 294.



CHECK

FOR

PRESCRIPTION

GRAHAME & MOORE

Pharmacists

BALTIMORE

For further detailed information regarding the numerous and often perplexing operations of the dispensing-counter, the reader is referred to two excellent books, containing much valuable information, namely, *The Art of Compounding*, by Prof. W. L. Scoville, of Boston, and *The Art of Dispensing*, by P. MacEwan, Esq., of London, England (6th edit.).

PART III.

PHARMACEUTICAL CHEMISTRY.

ALTHOUGH the term *pharmaceutical chemistry* is objected to by many who rightfully claim that there can be but one kind of chemistry, the laws and principles of which must be the same whether applied to pharmacy, medicine, physiology, or agriculture, it will, nevertheless, be retained in this book as a convenient heading under which to group the many details of composition, preparation, and examination of that vast number of chemical compounds in almost daily use by pharmacists, and the majority of which are officially recognized in the U. S. Pharmacopœia. The classification of chemical compounds with regard to constitution, etc., will, in the main, not be based upon the views at present accepted by chemists, concerning which the student of pharmacy receives ample instruction in his chemical lectures, and of which he can find full explanation in the many excellent chemical text-books of to-day; but a somewhat unsystematic arrangement will be followed, having in view more particularly the study of official and other chemicals from a pharmaceutical standpoint irrespective of their chemical relationship. After an experience of many years this plan, being still found the most desirable for pharmacists, is adhered to in pharmaceutical schools.

Chemical compounds may be conveniently divided into those usually designated as inorganic substances and those formerly known as organic compounds, but to which now the name carbon compounds is more appropriately applied.

INORGANIC SUBSTANCES.

Of the 15 elements which are known as non-metallic bodies, all but 6 are of pharmaceutical interest, either because they are employed extensively by physicians in their elementary state or because they form certain important compounds with each other which are officially recognized in the Pharmacopœia; such compounds only will be considered here, and these are furnished by the following elements: hydrogen, oxygen, chlorine, bromine, iodine, sulphur, phosphorus, carbon, and boron. A very valuable class of compounds formed by these elements are the inorganic acids, which will be treated in a separate chapter.

Combinations of non-metallic elements with the metals are very properly classified as compounds of the latter, and will be considered in connection with the salts and numerous other preparations of the metals, officially recognized. The compounds of metals may be conveniently considered according to a system which groups those metals together the oxides of which possess certain well-recognized properties in common; thus, metals of the alkalies, of the alkaline earths, of the earths and heavy metals.

Since very few metallic salts are prepared by pharmacists, such compounds will be treated chiefly with a view of enabling the student to understand fully the official requirements as regards identity and quality, detailed consideration being given mainly to those compounds for the preparation of which the Pharmacopœia gives official working formulas.

CHAPTER XXXVII.

HYDROGEN AND OXYGEN.

NEITHER hydrogen nor oxygen is of pharmaceutical value in its uncombined gaseous state, but they unite to form two very important compounds.

The most important compound of hydrogen and oxygen is water, which may be looked upon chemically as hydrogen monoxide, H_2O. The Pharmacopœia recognizes both natural and distilled water, and while in some localities natural water may be obtained remarkably free from impurities, the use of distilled water is to be preferred at the dispensing-counter and for the preparation of aromatic waters and many chemical solutions. While the official limit for the presence of inorganic impurities, as shown by the residue upon evaporation of the water, is fixed at $\frac{1}{20}$ per cent. (0.5 Gm. in 1000 Cc.) for natural water, it has been reduced to $\frac{1}{133}$ per cent. (0.075 Gm. in 1000 Cc.) for distilled water. Moreover, the Pharmacopœia requires that natural water mixed with 10 per cent. of its volume of diluted sulphuric and 0.4 per cent. of $\frac{N}{10}$ potassium permanganate solution shall not become completely decolorized by boiling it for 10 minutes, showing the limit of organic and other oxidizable substances; in the case of distilled water the complete absence of such oxidizable matter is demanded, and while only one-fourth as much potassium permanganate solution is to be added, the mixture, after having been boiled for 10 minutes, should not wholly lose its pink color if set aside in a dark place, covered, for 10 hours.

Hydrogen dioxide, H_2O_2, first obtained in 1818 by Thenard, contains 94 per cent. of oxygen, and is the richest oxygen compound known. It is officially recognized, in the form of a 3 per cent. aqueous solution, under the name Aqua Hydrogenii Dioxidi.

The compound H_2O_2 may be obtained from any metallic dioxide which yields a portion of its oxygen to water upon treatment with an acid. For technical purposes, sodium dioxide is extensively employed, but this method is not suitable for medicinal purposes, as the resulting solution cannot be freed from the accompanying sodium sulphate or chloride. The Pharmacopœia no longer gives directions for making solution of hydrogen dioxide. That intended for medicinal use is usually made from barium dioxide, which upon saturation with an acid readily gives up one-half of its oxygen to water

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to form hydrogen dioxide, as shown by the following equation: $6BaO_2 + 6H_2O + 4H_3PO_4 = 6H_2O_2 + 2Ba_3(PO_4)_2 + 6H_2O$.

An important step in the manufacture is the thorough hydration of the barium dioxide, in order to insure rapid and complete saturation subsequently with the acid; experience has shown that cold favors hydration of the finely powdered barium dioxide, which is known to be completed when the water separates but slightly from the resulting magma. Phosphoric acid has been found to produce a larger yield of H_2O_2 than sulphuric or carbonic acid, and is even preferable to hydrochloric acid, owing to the difficulty of removing the free acid after decomposition of the barium chloride formed. Hydrofluoric acid has also been successfully employed for the liberation of hydrogen dioxide, but its corrosive nature presents great obstacles to its use, although the resulting barium fluoride is even more insoluble than the phosphate. The hydrated barium dioxide must be fully decomposed and saturated with acid to exact neutrality; about 96 Cc. of phosphoric acid diluted with 320 Cc. of distilled water will be required for 300 Gm. of barium dioxide hydrated by addition to 500 Cc. of cold distilled water. A portion (about 50 Cc.) of the diluted acid is set aside as a reserve, and used in small quantities after all the barium dioxide mixture has been added to the remainder of the acid, until a perfectly neutral reaction is obtained. Vigorous agitation and refrigeration of the acid and barium mixture are necessary to insure a full yield of H_2O_2. After filtration of the mixture, an addition of small quantities of diluted sulphuric acid is made to the filtrate for the purpose of freeing it entirely from barium, a small portion of which will have entered into solution as acid barium phosphate; the newly formed precipitate of barium sulphate may be removed by filtration after addition of a little starch. The finished product contains a small amount of phosphoric acid, liberated from the acid phosphate, and a trace of sulphuric acid.

Solution of hydrogen dioxide readily undergoes spontaneous decomposition, particularly if exposed to heat and sunlight; it should, therefore, be preserved in a cool, dark place, or in amber-colored bottles which have been not too tightly stoppered, to avoid explosion in case of defective bottles and increased pressure caused by accumulation of gas. As a preservative, boroglycerin has been suggested; and when used in the proportion of 1 part in 100 of the solution, has been found serviceable in retarding decomposition. Moderate heat is far less injurious than daylight; and Dr. Squibb found that if a temperature of 60° C. (140° F.) be not exceeded, a 50-volume solution can readily be obtained by concentration on a water-bath without appreciable loss of dioxide; above this temperature, however, decomposition rapidly increases.

The Pharmacopœia requires that solution of hydrogen dioxide shall contain 3 per cent. by weight of the pure dioxide, which corresponds to about 10 volumes of available oxygen. The assay is made with potassium permanganate, in the presence of sulphuric acid, according to the reaction $5H_2O_2 + 3H_2SO_4 + 2KMnO_4 = K_2SO_4 + 2MnSO_4 + 8H_2O + 5O_2$. Only one-half of the oxygen indicated in the equation is derived from the hydrogen dioxide, the other half being furnished by the potassium permanganate, which fact must be considered if the gas is collected and measured in a gas-tube over mercury. The term available oxygen refers, therefore, to the volume of nascent oxygen obtained directly from the dioxide, and not to the total volume liberated in the reaction. From the above equation it is seen that 2 molecules (313.96 parts) of potassium permanganate correspond to 5 molecules (168.8 parts) of hydrogen dioxide; hence each Cc. of a $\frac{N}{10}$ solution of the former containing 0.0031396 Gm. of $KMnO_4$ must be equivalent to 0.001688 Gm. of H_2O_2, or 0.000794 Gm. of oxygen available therefrom.

Thus the volume strength of any solution of hydrogen dioxide can be conveniently calculated simultaneously with the percentage strength, without the necessity of collecting and measuring the actual gas volume, by reckoning the weight of 1 Cc. of oxygen at 0° C. and 760 Mm. atmospheric pressure as equivalent to 0.001423 Gm. (actually 0.00142293 +); then, dividing the weight of oxygen equivalent to 1 Cc. of $\frac{N}{10}$ $KMnO_4$ solution, 0.000794 Gm. (as shown above), by 0.001423, we obtain 0.56 Cc. (actually 0.55794) as the volume of oxygen represented by each Cc., and multiplying the number of Cc. $\frac{N}{10}$ $KMnO_4$ solution decolorized by 1 Cc. of H_2O_2 solution by 0.56, the volumes of available oxygen are indicated by the product. If 10 Cc. of solution of hydrogen dioxide be diluted with sufficient water to 100 Cc., and of this liquid 16.9 (strictly speaking, 16.88) Cc., representing 1.69 (1.688) Cc. of the original solution, be used for the assay as officially directed, each Cc. of the tenth-normal potassium permanganate solution consumed corresponds to 0.1 per cent. of absolute H_2O_2; the number of Cc. of potassium permanganate solution decolorized in the official assay, if multiplied by 0.1, will therefore express the percentage of hydrogen dioxide present in the sample.

The reaction with potassium chromate and ether mentioned in the Pharmacopœia depends upon the formation of a new compound which forms a blue solution with ether; it is characteristic of hydrogen dioxide. By some the compound formed is considered to be perchromic anhydride (Cr_2O_7), a substance analogous to permanganic anhydride (Mn_2O_7), while others assume that it may possibly be a compound of CrO_3 and H_2O_2.

CHAPTER XXXVIII.

CHLORINE, BROMINE, AND IODINE.

Chlorine in its elementary state is used by physicians in the form of an aqueous solution, which in the present Pharmacopœia is recognized under the name Liquor Chlori Compositus (Compound Solution of Chlorine) and for the preparation of which an official formula is given. It is defined to be a solution containing, when freshly prepared, about 0.4 per cent. of chlorine, with some oxides of chlorine and potassium chloride. Although the Pharmacopœia includes the name *chlorine water* among the official English titles of this preparation, the latter by no means corresponds to the chlorine water of foreign and former United States Pharmacopœias, and should not be used when chlorine water is intended as a chemical reagent.

Compound solution of chlorine is intended for internal administration of chlorine, and the official formula makes the extemporaneous preparation of the solution an easy task. When moderately dilute, hydrochloric acid is allowed to act upon potassium chlorate, as directed in the official process; a greenish-yellow gas is formed, which has been called euchlorine, and is a mixture of chlorine and chlorine dioxide. The reaction occurring may be shown by the following equation: $2KClO_3 + 4HCl = 2KCl + 2H_2O + 2ClO_2 + Cl_2$. Care is necessary in adding the distilled water in divided portions, to guard against the loss of chlorine gas when inserting the stopper prior to agitating the flask. The finished solution is a liquid of almost golden-yellow color and a strong chlorine odor. It retains its color for some time, and should be preserved in small well-filled bottles, well-stoppered and paraffined, and kept in a dark place.

If pure chlorine water is wanted for use in chemical operations or otherwise, it may be prepared by heating pure hydrochloric acid, moderately diluted with water, in a flask with an excess of manganese dioxide in lumps of about the size of filberts, the gas evolved being passed through a small quantity of water contained in a wash bottle and then into a larger volume of distilled water kept at a temperature not above 10° C. (50° F.) until a saturated solution is obtained. The object of previously washing the gas is to remove any hydrochloric acid vapors that may have escaped along with the chlorine. Such chlorine water deteriorates rapidly when exposed to air and light, but can be preserved for a considerable time if kept in small bottles, well-filled and tightly stoppered and paraffined, in a cool, dark place.

When preparing chlorine-water, sulphurous acid, and similar solutions, it may happen that, owing to cessation or interruption of the gas-flow, a partial vacuum is produced in the generating flask, and, as a consequence, liquid from the wash-bottle is drawn over into the flask, and, coming in contact with the heated glass, will cause a fracture. This may be avoided either by using a safety-tube or by disconnecting the flask from the wash-bottle as soon as gas-bubbles cease to pass over.

Bromine is employed in its free state as an antiseptic and disinfectant, and is occasionally used internally as an alterative. It is a heavy, dark brownish-red liquid, which even at ordinary temperatures evolves a highly irritating vapor; hence considerable care is necessary in handling bromine. A vial of bromine should be well cooled before opening, especially in warm weather, to avoid accidents; and if large quantities are to be used, as in the manufacture of syrup of ferrous bromide and similar preparations, it is best to open the vial under ice-water. Contact of bromine or its vapor with metallic surfaces must be carefully avoided.

The manufacture of bromine has rapidly increased during the last thirty-five years, and immense quantities of it are now produced in this country. It occurs in nature, in aqueous solution, combined with sodium, magnesium, and calcium, and is present in sea-water to the extent of about $\frac{1}{175}$ of 1 per cent. The commercial sources of bromine are the mother-liquors left after the crystallization of sodium chloride at the salt wells of Ohio, Pennsylvania, West Virginia, and Michigan, in this country, and near Stassfurt, in Germany. Since the bromides are far more soluble than the chlorides, the former remain in solution in the mother-liquors, to which the name bittern is given in this country. The bittern is concentrated until a density of about 1.45 is reached, which facilitates the further removal of chlorides and sulphates, then transferred to stoneware stills, where a mixture of sulphuric acid and manganese dioxide is added, which, with the aid of heat, liberates the bromine according to the following reaction: $MgBr_2 + MnO_2 + 2H_2SO_4 = Br_2 + MgSO_4 + MnSO_4 + 2H_2O$. The bromine vapor is condensed in well-cooled receivers and freed from water by distillation over calcium chloride.

Bromine is soluble in 28 parts of water at 25° C. (77° F.), but its solubility is materially increased by the presence of potassium bromide. The Pharmacopœia directs bromine water, for use as a test-solution, to be made by dissolving 1 Cc. of bromine in sufficient water to make 100 Cc. of solution. It changes readily, but is more permanent than chlorine water, and should be kept in a dark place.

It is difficult to obtain bromine entirely free from chlorine, the plan usually followed being distillation with a bromide, whereby the corresponding chloride is formed and bromine set free. The Pharmacopœia demands that bromine shall contain not more than 3 per cent. of impurities, but no method is given for ascertaining the percentage of actual purity. The chief impurity, as stated above, is chlorine, and the equation $Ba + Cl_2 = BaCl_2$ shows that 2 atoms or 70.36 Gm. of chlorine are capable of forming 1 molecule or 206.76 Gm. of anhydrous barium chloride; hence 1 Gm. of chlorine will form 2.938 + Gm. of the salt, or 0.01 Gm. will form 0.0294 (actually 0.02938 +) Gm. Advantage may be taken of this fact in determining the exact amount of chlorine in any sample of bromine by the following method: Mix 1 Gm. of bromine with 10 Cc. of distilled water, adding sufficient ammonia water to produce a clear solution, then digest with barium carbonate, filter, evaporate the filtrate to dryness, and gently ignite the saline residue. The latter should be soluble in absolute alcohol, and every 0.0294 Gm. of insoluble residue will indicate 1 per cent. of chlorine, barium chloride being insoluble, while the bromide is soluble in absolute alcohol.

Bromoform and other organic impurities may be present and are derived in part at least from the luting and fastenings of the stills; their absence is indicated by adding bromine to an excess of potassium hydroxide solution, when a permanently clear solution should result without the separation of oily drops. Iodine is rarely present, but, if so, will be liberated by ferric chloride, if the latter be added to a solution of bromine previously shaken with reduced iron until nearly colorless, and may be detected with the aid of starch; the reaction is as follows: $FeI_2 + 2FeCl_3 = 3FeCl_2 + I_2$.

Bromine has been found an efficient antidote to the poison of the rattlesnake, and the following formula for *Bibron's Antidote* is taken from Parrish's *Pharmacy*, published in 1884: Dissolve 5 drachms (300 grains) of bromine in 6 fluidounces of diluted alcohol and 4 grains of potassium iodide and 2 grains of mercuric chloride in $1\frac{1}{2}$ fluidounces of diluted alcohol; mix the two solutions. Dose: 10 drops in a tablespoonful of brandy, to be repeated as required.

Iodine is more extensively employed in its elementary state than any other element, both internally and externally. It was formerly derived solely from the ashes of sea-plants, particularly of certain species of Laminaria. These ashes are known on the coast of Scotland, where at one time the chief iodine manufactories were located, as *kelp*, in Norway as *varec*, and in Spain as *barilla;* they contain iodine in the form of alkali iodides, NaI and KI. After treatment with water the chlorides, carbonates, and sulphates present are removed by evaporation of the solution and crystallization; sulphuric acid is then added to decompose sulphides and other sulphur compounds; to the acid liquid, manganese dioxide is added, and the mixture is heated. The iodine, volatilizing, passes into suitable condensing flasks and sublimes, a reaction similar to that stated under chlorine and bromine taking place.

At present vast quantities of iodine are obtained in South

America from the mother-liquors of the so-called Chili saltpetre, sodium nitrate, which contains iodine in the form of sodium iodate. The iodine is obtained either by direct precipitation with sodium bisulphite and sulphur dioxide or by sublimation, after addition of manganese dioxide and sulphuric acid to cuprous iodide, which has been previously precipitated from a solution of sodium iodide by cupric and ferrous sulphates. The chemical reactions involved in these two processes can be seen from the following equations:

By direct precipitation:

$$2NaIO_3 + 4NaHSO_3 + SO_2 = 4NaHSO_4 + Na_2SO_4 + I_2.$$

By sublimation, from cuprous iodide:

$$(1)\quad NaIO_3 + 3NaHSO_3 = 3NaHSO_4 + NaI.$$

$$(2)\quad 2NaI + 2CuSO_4 + 2FeSO_4 = Cu_2I_2 + Na_2SO_4 + Fe_2(SO_4)_3.$$

$$(3)\quad Cu_2I_2 + 2MnO_2 + 4H_2SO_4 = 2CuSO_4 + 2MnSO_4 + I_2 + 4H_2O.$$

The crude iodine thus obtained is freed from moisture and purified by resublimation. Commercial iodine may contain, as impurities, cyanogen, chlorine, and bromine, present as CNI, ICl_3, and IBr. The Pharmacopœia demands the absence of iodine cyanide, which is a very poisonous compound, and limits the amount of chlorine and bromine. In the official test for iodine cyanide, a further addition of a drop of ferric chloride test-solution, made before adding the sodium hydroxide solution, would render the reaction more intense, as it depends upon the formation of ferric ferrocyanide, $Fe_4(FeC_6N_6)_3$, which, if present in sufficient quantity, will settle as a blue precipitate, otherwise only a blue color is imparted to the liquid. The official limit-test for chlorine and bromine depends upon the greater solubility of silver chloride and bromide in ammonia water and their subsequent precipitation upon the addition of nitric acid.

The Pharmacopœia requires 99 per cent. purity for iodine, which is volumetrically determined with $\frac{N}{10}$ sodium thiosulphate solution, each Cc. of which corresponds to 0.01259 Gm. of iodine. If 0.50 Gm. of iodine be used for the valuation, as directed in the Pharmacopœia, 39.32 Cc. of the thiosulphate solution will be required to decolorize the liquid completely; for 99 per cent. of 0.50 is equal to 0.4950, and 0.4950 divided by 0.01259 yields 39.31 +. The exact percentage of purity may be ascertained by multiplying the number of Cc. of tenth-normal sodium thiosulphate solution consumed by 1.259 (0.01259 × 100) and dividing the product by the weight of iodine used in the test. The reaction involved may be explained by the following equation, $2\,(Na_2S_2O_3 + 5H_2O) + I_2 = 2NaI + Na_2S_4O_6 + 10H_2O$, sodium iodide and sodium tetrathionate being formed, both of which yield colorless solutions.

One solid and two liquid preparations containing iodine in a free state are recognized in the Pharmacopœia, namely: an alcoholic solution designated as tincture of iodine, containing 7 Gm. of iodine and

5 Gm. of potassium iodide in 100 Cc.; an aqueous solution known as Lugol's Solution, containing 5 per cent. by weight of iodine held in solution by twice its weight of potassium iodide; and an ointment containing 4 per cent., by weight, of iodine. The amount of iodine present in any sample of the tincture or compound solution can be readily determined by titration with sodium thiosulphate.

Three other liquid preparations of iodine are used by physicians, known respectively as Churchill's iodine caustic, Churchill's tincture of iodine, and decolorized tincture of iodine; formulas for the three solutions are given in the *National Formulary*. The first-named consists of iodine 25 Gm., potassium iodide 50 Gm., water 100 Cc.; the second-named contains in 100 Cc. iodine 16.5 Gm., potassium iodide 3.3 Gm., water 25 Cc., and sufficient alcohol to make the prescribed volume. Decolorized tincture of iodine is not a solution of iodine at all, the name being misapplied; the finished colorless product contains sodium iodide, sodium tetrathionate, and ammonium iodide, formed by reaction between iodine, sodium thiosulphate, and ammonia water. The preparation in a short time acquires a disagreeable alliaceous odor and deposits crystals of sodium tetrathionate, which may be removed by filtration.

Iodine forms with hydrogen an important compound, hydriodic acid, which in the form of a diluted solution is recognized in the Pharmacopœia, and from which in turn the official syrup of hydriodic acid is made. The former solution is of 10 per cent. acid strength and the latter of 1 per cent. strength, which in both cases is determined volumetrically by means of $\frac{N}{10}$ silver nitrate solution, as explained under Diluted Hydriodic Acid.

CHAPTER XXXIX.

SULPHUR, PHOSPHORUS, CARBON, AND BORON.

Sulphur is found widely diffused, both in the free state and in combination. While by far the greater portion of sulphur used in this country comes from Italy, it is now also mined in the States of California, Nevada, and Utah, a bed of sulphur 2000 feet square and over 60 feet thick existing in the latter State. Commercially, sulphur occurs in four varieties, namely, that known as stick or roll sulphur, chiefly used for fumigation and bleaching; and sublimed, washed, and precipitated sulphur, extensively used in medicine. Roll sulphur, known also as brimstone, is prepared by heating the crude sulphur obtained from various sources, allowing impurities to settle and pouring the fused sulphur into cylindrical moulds, in which it is allowed to congeal.

Sublimed Sulphur, as its name indicates, is obtained by vaporizing sulphur and passing the vapor into large stone or brick chambers, the temperature of which is not allowed to rise above 100° or 110° C. (212° or 230° F.), where the sulphur is deposited in partly crystalline and partly amorphous particles, known as flowers of sulphur. The two varieties can be separated from each other by treatment with carbon disulphide, which dissolves the crystalline but not the amorphous sulphur. In boiling solutions of alkali hydroxides sulphur is perfectly soluble, forming such compounds as alkali pentasulphide and thiosulphate. Nearly all sulphur is contaminated with arsenic, and this, as arsenic tersulphide, As_2S_3, together with traces of selenium and some sulphuric acid formed by oxidation, are the usual impurities found in sublimed sulphur. Not more than 0.5 per cent. of fixed impurities should remain upon ignition. Sublimed sulphur shows an acid reaction when water is shaken with it and then tested with blue litmus paper.

Washed Sulphur is recognized in the Pharmacopœia as Sulphur Lotum, and is prepared by digesting sublimed sulphur with diluted ammonia water. This treatment removes any sulphuric acid and arsenic sulphide present as ammonium sulphate, arsenite, and sulpharsenite, according to the following reaction: $H_2SO_4 + As_2S_3 + 8NH_4OH = (NH_4)_2SO_4 + (NH_4)_3AsO_3 + (NH_4)_3AsS_3 + 5H_2O$. The mixture is subsequently strained, and the resulting purified sulphur is washed with cold water to remove excess of ammonia; it is finally dried thoroughly with the aid of moderate heat, so as to prevent oxidation. The Pharmacopœia demands that washed sulphur shall contain not less than 99.5 per cent. of pure sulphur, and that upon volatilization or ignition it shall not leave more than 0.2 per cent. of residue. When shaken with water, the latter should affect neither blue nor red litmus paper, showing the absence of both acid and ammonia.

Precipitated Sulphur, also known as lac sulphuris or milk of sulphur, is made from sublimed sulphur by first uniting this to an alkali and then decomposing the resulting compound with an acid. Milk of lime is preferred mainly on account of its cheapness; upon boiling it with sulphur both pentasulphide and thiosulphate are obtained in solution, thus: $12S + 3CaO = 2CaS_5 + CaS_2O_3$. The Pharmacopœia directs that hydrochloric acid shall be added to the clear filtrate until the latter is nearly neutralized, but still exhibits an alkaline reaction; this is partly to avoid decomposition of the calcium thiosulphate, which would yield sulphur insoluble in carbon disulphide and in a coarser state of division, and partly to prevent the precipitation of any arsenic trisulphide, for, if arsenic had been present in the sublimed sulphur, it would have formed calcium sulpharsenate, $Ca_3As_2S_8$, which is soluble in the alkaline liquid, but is decomposed by acids. The official process causes a decreased yield of precipitated sulphur, but a purer product, the final reaction being only between the calcium pentasulphide and hydrochloric acid. Sulphuric acid is sometimes used in place of hydrochloric acid, but is not permissible, since it would contaminate the sulphur with insoluble calcium sulphate, whereas hydrochloric acid yields calcium chloride, easily removable by washing.

Sulphur forms two compounds with iodine, a monoiodide, S_2I_2, and a hexiodide, SI_6; only the former is of interest to pharmacists, as it is sometimes used by physicians in the form of an ointment. It contains 20 per cent. of sulphur and 80 per cent. of iodine. The official directions for making sulphur iodide are very simple; and, as union of the two elements takes place at a moderately elevated temperature, loss of iodine can be easily avoided. The compound must be preserved in well-stoppered vials, as it readily decomposes when exposed to the air; the union is not a very strong one, as boiling water is capable of abstracting all the iodine from the compound.

Phosphorus occurs in nature chiefly as calcium phosphate, which makes up the structure of bone and is found as extensive mineral deposits. Pure phosphorus is obtained by distilling calcium metaphosphate with sand and charcoal. Owing to its great avidity for oxygen and ready inflammability, it must be preserved under water, and care is necessary in handling it. Elementary phosphorus is used to a considerable extent in medicine, in the form of the official and other pills. The elixir and spirit of phosphorus are no longer recognized in the Pharmacopœia; neither is phosphorated oil.

Carbon is recognized in the Pharmacopœia in the form of wood charcoal and animal charcoal; the former will be considered in connection with the products of woody fibre (see Cellulose). Animal charcoal is extensively employed as a decolorizing agent by manufacturing chemists; it is prepared by roasting bones in iron cylinders until vapors cease to be given off; the residuary charcoal, mixed with large proportions of inorganic constituents, is known in its crude state as bone-black. Meat and blood are also made to yield animal charcoal by a somewhat similar process. Purified animal charcoal differs from crude bone-black in having been repeatedly treated with boiling diluted hydrochloric acid, whereby all acid-soluble impurities, such as calcium carbonate and phosphate, are removed. By this treatment animal charcoal loses about 80 per cent. in weight, leaving a small proportion (4 per cent.) of siliceous matter mixed with the purified charcoal. If not completely carbonized, animal charcoal will impart color to water if boiled with the same in the presence of potassium hydroxide. The remarkable decolorizing property of animal charcoal is due to the very fine state of division of the carbon and its consequent increased surface attraction. While crude animal charcoal is largely used for neutral solutions in the arts, only the purified article should be employed for acid liquids or delicate chemical solutions. So-called spent charcoal, charged with organic matter, can be regenerated by appropriate heating.

The only preparation of carbon to be considered is carbon disulphide, CS_2, which is not employed medicinally, but is a valuable solvent for caoutchouc, fats, and many other substances. It is prepared by direct union of charcoal and sulphur, vapors of the latter being passed over the former heated to redness, and then condensed in suitable receivers. It is freed from dissolved sulphur by distillation on a water-bath, while hydrogen sulphide, which is also formed, is removed by agitation with mercury; the liquid is further rectified by distillation with wax or fat, whereby certain offensive sulphur compounds are removed. When exposed to light, carbon disulphide assumes a yellow color and acquires a fetid odor, owing to decomposition. The Pharmacopœia demands the absence of dissolved sulphur, hydrogen sulphide, and sulphur dioxide.

Boron is never used in pharmacy or medicine in its free state. Its compound with oxygen, boric acid, will be considered in the following chapter.

CHAPTER XL.

THE INORGANIC ACIDS.

INORGANIC acids, which are extensively employed by pharmacists, and therefore of great importance, are combinations of nonmetallic elements with hydrogen and oxygen, and in a few cases with hydrogen alone. The presence of hydrogen lends to these compounds their peculiar acid character. Compounds with oxygen only, possess no acid properties, and are termed anhydrides or simply oxides; they, however, unite chemically with water to form well-defined acids; thus we have sulphurous and sulphuric anhydrides, SO_2 and SO_3, known also as sulphur dioxide and trioxide, which, combining with water, yield sulphurous and sulphuric acids, as $SO_2 + H_2O = H_2SO_3$ and $SO_3 + H_2O = H_2SO_4$; carbon dioxide, CO_2, in contact with water, yields carbonic acid, H_2CO_3; nitric anhydride, or nitrogen pentoxide, N_2O_5, yields nitric acid, HNO_3, thus $N_2O_5 + H_2O = 2HNO_3$; phosphoric anhydride or phosphorus pentoxide, P_2O_5, will yield with water phosphoric acid, H_3PO_4, thus $P_2O_5 + 3H_2O = 2H_3PO_4$, etc.

Acids are characterized by a sour taste, the property of changing the color of blue litmus-paper to red, of neutralizing alkalies, and of forming with these and other bases well-defined salts. The salts thus formed are not always neutral compounds, which fact is due to different basicity of the various acids, depending upon the number of replaceable hydrogen atoms present in the acid; hence the terms mono-, di-, tri-, and tetrabasic, referring to the presence of 1, 2, 3, or 4 atoms of hydrogen, which can be replaced by as many basylous atoms or groups, giving rise to normal and acid salts. Normal salts are such as are formed by complete saturation of an acid by a base, or, in other words, they are produced whenever all the replaceable hydrogen of an acid is replaced by a base; acid salts, on the other hand, still retain a part of the replaceable hydrogen of acids, and are the result of imperfect neutralization of an acid by a base. (Examples, KNO_3 and Na_2SO_4 are normal salts, while $NaHCO_3$ and KH_2PO_4 are acid salts.) Monobasic acids never form acid salts. In the pharmacopœial chemical formulas for acids the replaceable hydrogen is stated first, hence the basicity of the acid can be seen at a glance; thus hydrochloric, hydrobromic, hypophosphorous, and nitric acids are all monobasic, sulphurous and sulphuric acids are dibasic, while boric and phosphoric acids are tribasic.

Both crude and purified acids are offered for sale by manufacturers; the former, while suitable for many technical purposes, should never be used for pharmaceutical preparations. A very important point in connection with inorganic acids is the percentage of absolute acid present in the commercial solutions sold under their respective names. The Pharmacopœia, in every instance, designates the percentage strength of the official acids, and pharmacists should insist on being furnished such acids by manufacturing chemists; the designation C. P. (chemically pure), placed on the labels of acid bottles, is no clue as to the strength of the solution; either the initials U. S. P. or the percentage of absolute acid should be stated. Manufacturing chemists will not be slow in recognizing the justice of such a demand if pharmacists insist upon it; otherwise the same uncertainty as to strength will continue. All working formulas of the Pharmacopœia, requiring the use of inorganic acids, are based upon the assumption that acids of official strength will be used. Absolute purity is not demanded for official acids, for, while this is essential for chemical reagents, it is considered unnecessary for medicinal acids, and, if insisted upon, would greatly enhance the cost of the article without adding to the value of the acid for medicinal or pharmaceutical purposes. Certain impurities, which it would be difficult to remove entirely except at considerable expense, are allowed by the Pharmacopœia to be present within prescribed limits. As different acids have different saturating powers, the official volumetric determinations are only useful in fixing the strength of the acid examined, after the absence of other acids has been proved by the tests prescribed for that purpose.

Only such inorganic acids will be considered here as are designated in the Pharmacopœia, and are therefore of special interest to the student of pharmacy. Details of the manufacture of the principal acids will not be essayed, as text-books on chemistry furnish all such information. While there must naturally exist a great diversity in the strength of the various so-called strong acids, the Pharmacopœia has fixed the proportion of absolute acid in all official diluted inorganic acids at 10 per cent., with the exception of diluted nitro-hydrochloric acid. With one exception, boric acid, all the official inorganic acids are liquid.

The following is a list of the official inorganic acids:

English Name.	Latin Name.
Boric Acid,	Acidum Boricum.
Diluted Hydriodic Acid,	Acidum Hydriodicum Dilutum.
Diluted Hydrobromic Acid,	Acidum Hydrobromicum Dilutum.
Hydrochloric Acid,	Acidum Hydrochloricum.
Diluted Hydrochloric Acid,	Acidum Hydrochloricum Dilutum.
Hypophosphorous Acid,	Acidum Hypophosphorosum.
Diluted Hypophosphorous Acid,	Acidum Hypophosphorosum Dilutum.
Nitric Acid,	Acidum Nitricum.
Diluted Nitric Acid,	Acidum Nitricum Dilutum.
Nitrohydrochloric Acid,	Acidum Nitrohydrochloricum.
Diluted Nitrohydrochloric Acid,	Acidum Nitrohydrochloricum Dilutum.
Phosphoric Acid,	Acidum Phosphoricum.

English Name.	Latin Name.
Diluted Phosphoric Acid,	Acidum Phosphoricum Dilutum.
Sulphuric Acid,	Acidum Sulphuricum.
Aromatic Sulphuric Acid,	Acidum Sulphuricum Aromaticum.
Diluted Sulphuric Acid,	Acidum Sulphuricum Dilutum.
Sulphurous Acid,	Acidum Sulphurosum.

Boric Acid. H_3BO_3 or $B(OH)_3$.—Boric acid, also known as boracic acid, occurs in nature both in a free and combined state, the free acid, in the form of vapor, issuing with steam from the earth in volcanic regions, particularly in Tuscany, Italy, while the combined acid is usually found as sodium tetraborate or borax. Medicinal boric acid is probably all obtained by decomposition of a boiling solution of borax with hydrochloric acid, which latter is preferable to sulphuric acid, as it can be more readily removed from the crystals of boric acid by washing; the reaction is a very simple one—$(Na_2B_4O_7 + 10H_2O) + 2HCl = 4H_3BO_3 + 2NaCl + 5H_2O$. When heated, boric acid gradually loses water and is converted into metaboric acid, HBO_2; with increasing temperature, into tetraboric acid, $H_2B_4O_7$; and, finally, above 160° C. (320° F.) all hydrogen is eliminated in the form of water and boron trioxide remains, thus $2H_3BO_3 = B_2O_3 + 3H_2O$.

The Pharmacopœia requires the absence of all impurities in boric acid except traces of iron. Its chief characteristics are that it imparts a green color to the flame of burning alcohol, and that it changes the yellow color of turmeric paper brown even in the presence of hydrochloric acid.

Diluted Hydriodic Acid.—An aqueous solution containing not less than 10 per cent. of absolute hydriodic acid and about 0.63 per cent. of hypophosphorous acid. It may be conveniently prepared by the official formula, which involves the decomposition of potassium iodide and hypophosphite by means of tartaric acid in hydroalcoholic solution. The reaction is shown by the following equation: $KI + KPH_2O_2 + 2H_2C_4H_4O_6 = HI + HPH_2O_2 + 2KHC_4H_4O_6$, from which it will be seen that 164.76 parts of potassium iodide will yield 126.9 parts of hydriodic acid, and 103.39 parts of potassium hypophosphite will yield 65.53 parts of hypophosphorous acid; hence the quantity of these salts directed in the official formula, 135 Gm. of the iodide and 10 Gm. of the hypophosphite, will yield 100 Gm. and 6.338 Gm. of hydriodic acid and hypophosphorous acid respectively. The use of alcohol in the process materially aids in the precipitation of the newly formed acid potassium tartrate, as does also the application of cold, the Pharmacopœia allowing not more than 1 per cent. of residue if the diluted acid be evaporated to dryness. Upon evaporation of the filtrate for removal of the alcohol it assumes a yellowish color when concentrated, but no iodine is liberated, and the liquid again becomes colorless when diluted with distilled water.

In the official assay all the hydriodic acid present is precipitated by $\frac{N}{10}$ silver nitrate solution added in excess, which excess is determined by subsequent titration with $\frac{N}{10}$ potassium sulphocyanate solution in the presence of some nitric acid, ferric ammonium sulphate being used as an indicator. Since each Cc. of the silver solution, containing 0.016869 Gm. of silver nitrate, is capable of precipitating 0.01269 Gm. of hydriodic acid, as shown by the equation $AgNO_3 + HI = AgI + HNO_3$, it will represent $\frac{1}{2}$ per cent. of the 2.54 Gm. of diluted acid used for the assay, and 20 Cc. will be necessary to show the required 10 per cent. The addition of nitric acid is made to prevent the discoloration of the liquid by the indicator. The latter shows a permanent reddish-brown color of ferric sulphocyanate immediately when all excess of silver nitrate has been precipitated as silver sulphocyanate.

Solutions of hydriodic acid decompose readily, especially when exposed to light, but such change is obviated by the presence of small quantities of hypophosphorous acid. In the author' s experience diluted hydriodic acid made by the official method has kept perfectly for over six months in diffused light.

Diluted Hydrobromic Acid.—An aqueous solution containing 10 per cent. by weight of absolute HBr. Pure hydrobromic acid is a gaseous compound, and is rather unstable. The medicinal acid is prepared by manufacturers usually of two strengths, 34 per cent. and 10 per cent., the former being the more economical article to purchase, as the requisite proportion of water to reduce it to the official acid can be easily added by the pharmacist, 10 Gm. of 34 per cent. acid mixed with 24 Gm. of distilled water yielding 34 Gm. of 10 per cent. acid. Hydrobromic acid can be obtained in several ways, but is usually made on a large scale by a method first suggested by Dr. Squibb. Moderately diluted sulphuric acid is poured slowly, and with constant stirring, into a hot saturated solution of potassium bromide, when the following decomposition takes place: $2KBr + H_2SO_4 = 3HBr + K_2SO_4$; after twenty-four hours the potassium sulphate has crystallized out, the solution of hydrobromic acid is poured off, and the crystals are slowly washed with ice-cold water to recover adhering acid. Finally, the acid liquid is distilled in a glass retort on a sand-bath nearly to dryness. Its strength is ascertained by titration with normal potassium hydroxide solution, and sufficient water added to produce either a 34 or 10 per cent. solution as desired.

For preparing small quantities of the official acid, the precipitation methods of Wade and Fothergill may be employed, which are based on the decomposition of potassium bromide with tartaric acid; thus $KBr + H_2C_4H_4O_6 = HBr + KHC_4H_4O_6$. 11.9 Gm. of potassium bromide and 15 Gm. of tartaric acid are each dissolved in 30 Cc. of cold distilled water; the acid solution is poured into the saline solution, and the mixture, after having been well shaken for five or ten minutes, is placed in ice-water or an ice-chest for twenty-four or thirty-six hours; it is then filtered, and the vessel and filter carefully washed with ice-water until the filtered liquid weighs 81 Gm. A small quantity of acid potassium tartrate is likely to remain in the diluted acid prepared by this method.

The official acid has a specific gravity of about 1.076 at 25° C. (77° F.). The Pharmacopœia excludes all impurities except slight traces of hydrochloric acid and chlorides, and directs that 8.04 Gm. of the official diluted acid shall be neutralized exactly with ammonia water and then titrated with $\frac{N}{10}$ $AgNO_3$ solution, using potassium chromate as indicator; not less than 10 Cc. of the silver solution shall be required to impart a permanent red tint to the liquid. All hydrobromic acid present is precipitated as silver bromide, after which silver chromate of blood-red color is formed, which is soluble in acid as well as alkaline liquids, and hence the necessity of exactly neutralizing the diluted acid. Each Cc. of the silver solution is capable of precipitating 0.008036 Gm. of pure HBr., which corresponds to 1 per cent. of the 0.804 Gm. taken for the assay. The reason for determining the hydrobromic acid by precipitation with silver nitrate, instead of simply neutralizing it with normal alkali, is that hydrobromic acid frequently contains other acids, in which case the neutralization test would yield wrong results as far as the percentage of absolute hydrobromic acid is concerned.

Hydrochloric Acid.—This acid may be prepared quite pure by decomposing sodium chloride with pure sulphuric acid and conducting the gas into water. The crude acid of commerce is often obtained as a by-product in the manufacture of sodium or potassium carbonates from the respective chlorides; since sulphates are first made in this process by acting on the chlorides with sulphuric acid, the reactions are the same in the manufacture of crude and pure acid, and possibly occur in two distinct steps, namely: 1. $NaCl + H_2SO_4 = HCl + NaHSO_4$. 2. $NaCl + NaHSO_4 = HCl + Na_2SO_4$. The crude acid of commerce, better known as muriatic acid, is often of a deep-yellow color, owing to organic matter and traces of iron in solution; it should not be employed for pharmaceutical preparations.

Official hydrochloric acid should be free from all impurities except a bare trace of non-volatile substances and arsenic, the latter derived in all probability from the sulphuric acid. It has a specific gravity of about 1.158 at 25° C. (77° F.), and should contain 31.90 per cent. by weight of absolute HCl, which is determined by titration with normal KOH solution. As it is more convenient to measure small quantities of strong hydrochloric acid, the Pharmacopœia directs that 3 Cc. be weighed accurately in a stoppered weighing bottle, diluted with 50 Cc. of water and then titrated, methyl orange being used as an indicator. As each Cc. of the normal alkali solution is capable of neutralizing 0.03618 Gm. of absolute hydrochloric acid, the number of Cc. required in the official assay, when multiplied by 3.618 (0.03618×100) and then divided by the weight of the acid taken, will express the percentage of absolute acid present in the sample.

Strong hydrochloric acid usually causes white fumes when exposed to the air, due to the moisture in the air, and if ammonia be present white fumes of ammonium chloride will also be formed.

Diluted Hydrochloric Acid.—It is made from the official acid by mixing it with distilled water, in the proportion of 10 parts of the former to 21.9 parts of the latter, by weight, or, as the Pharmacopœia gives it, 100 Gm. of the acid with 219 Gm. of distilled water. This must yield a liquid containing 10 per cent. of absolute HCl, for the 100 Gm. of official hydrochloric acid contain 31.90 per cent. of HCl, and 31.90 Gm. are equal to 10 per cent. of 319 Gm. Diluted hydrochloric acid has a specific gravity of about 1.049 at 25° C. (77° F.), and corresponds in all its properties, reactions, and tests to the official stronger acid, except that it is odorless and produces no fumes when exposed to the air, and that 3.62 Gm. require only 10 Cc. of normal KOH solution of neutralization.

Hypophosphorous Acid.—The official acid liquid recognized under this name is an aqueous solution containing 30 per cent. of absolute hypophosphorous acid. It may be prepared by decomposing a solution of calcium hyphophosphite with oxalic acid, or by the method given in the *National Formulary*, which consists in mixing a strong aqueous solution of potassium hypophosphite with a hydroalcoholic solution of tartaric acid. The equation $KPH_2O_2 + H_2C_4.H_4O_6 = HPH_2O_2 + KHC_4H_4O_6$ shows that one molecule or 103.39 parts of absolute (or 105.4 parts of the official 98 per cent.) potassium hypophosphite will yield one molecule or 65.53 parts of absolute hypophosphorous acid, and hence to make 100 Gm. of the 30 per cent. acid will require 48.3 Gm. of the official potassium salt and 68.2 Gm. of tartaric acid, the former being dissolved in 50 Cc. of distilled water, and the latter in 100 Cc. of diluted alcohol. The mixture is well shaken and placed in an ice-bath for several hours and then filtered, the precipitated acid potassium tartrate being well washed with diluted alcohol. After concentration of the filtrate and washings to remove the alcohol, sufficient distilled water is added to bring the weight of the cold liquid up to 100 Gm.

Official hypophosphorous acid is a colorless liquid having a specific gravity of 1.130 at 25° C. (77° F.). Its strength is determined by titration with normal potassium hydroxide solution, each Cc. of which corresponds to 0.06553 Gm. of the absolute acid, methyl orange being used as an indicator. If 10 Gm. of hypophosphorous acid be diluted with water to measure 100 Cc. and then 65.5 Cc. of this solution, representing 6.55 Gm. of the original acid, be titrated, not less than 30 Cc. of normal alkali solution should be required for neutralization, showing 30 per cent. of absolute acid, each Cc. of the alkali solution corresponding to 1 per cent. of the acid.

This stronger acid is used almost entirely for manufacturing purposes and for the preparation of the official diluted acid, and it is necessary to guard against confusion of the two liquids. Manufacturing chemists have also placed on the market hypophosphorous acid containing 50 per cent. of the absolute acid.

Diluted Hypophosphorous Acid.—This acid solution is of only one-third the strength of the preceding and is directed by the Pharmacopœia to be made by mixing 1 part by weight of the 30 per cent. hypophosphorous acid with 2 parts by weight of water, and will then contain 10 per cent. of absolute acid. Its specific gravity is about 1.042 at 25° C. (77° F.) and it corresponds in all respects with the stronger acid, except that, if titrated with normal alkali solution exactly as stated above under the stronger acid, only 10 Cc. of the alkali solution will be required for neutralization. The chief use of this acid in pharmacy is as a preservative in certain chemical solutions prone to change by oxidation, such as diluted hydriodic acid, syrup of ferrous iodide, etc., as it possesses strong reducing properties.

Nitric Acid.—When potassium or sodium nitrate is treated with sulphuric acid, nitric acid is liberated, and may be condensed in suitable receivers. The reaction, in the case of potassium nitrate, occurs as follows: $KNO_3 + H_2SO_4 = HNO_3 + KHSO_4$; in the case of Chili saltpetre, provided a sufficient quantity of sodium nitrate be used, two distinct reactions may be said to occur, namely: 1. $NaNO_3 + H_2SO_4 = HNO_3 + NaHSO_4$; 2. $NaHSO_4 + NaNO_3 = HNO_3 + Na_2SO_4$. Sodium nitrate affords a larger yield than potassium nitrate, since the acid sodium sulphate reacts with the undecomposed nitrate at a much lower temperature than the acid potassium sulphate, the latter requiring a temperature at which the nitric acid is likely to be decomposed.

The Pharmacopœia demands absolute purity for nitric acid. If exposed to sunlight, the acid soon undergoes decomposition, a red color being imparted to the liquid, due to the formation of nitrogen tetroxide, N_2O_4; hence the acid must be kept in a dark place. Nitric acid of different strengths is placed upon the market by manufacturing chemists, ranging from 1.21 to 1.50 specific gravity; hence care is necessary to obtain the only kind recognized by the Pharmacopœia, which contains 68 per cent. of absolute HNO_3 and has a specific gravity of 1.403 at 25° C. (77° F.), otherwise considerable annoyance may be experienced when nitric acid is to be used as an oxidizing agent in any of the official preparations.

Nitric acid, being the most corrosive of the official acids, requires care in handling; in contact with the skin, it acts chemically on the same and produces a deep-yellow stain, this behavior, characteristic of nitric acid with albuminoid substances, being known as the xanthoproteic reaction.

The strength of nitric acid is determined exactly as in the case of hydrochloric acid, each Cc. of normal potassium hydroxide solution corresponding to 0.06257 Gm. of absolute nitric acid; hence the number of Cc. of normal alkali solution required to neutralize any given weight of nitric acid, when multiplied by 6.257 (0.06257 × 100) and the product divided by the weight of the acid taken will express the percentage of absolute nitric acid in the sample.

The so-called nitrous acid of commerce is simply nitroso-nitric acid —that is, nitric acid containing variable amounts of nitrogen tetroxide.

Diluted Nitric Acid.—This is made by diluting official nitric acid with distilled water in the proportion of 100 Gm. of the former to 580 Gm. of the latter, and must, therefore, contain 10 per cent. of absolute HNO_3, 100 Gm. of official acid containing 68 Gm., which are equal to 10 per cent. of 680 Gm., the total weight of the finished product. It has a specific gravity of about 1.054 at 25° C. (77° F.), and 6.26 Gm. should require 10 Cc. of normal KOH solution for complete neutralization.

Nitrohydrochloric Acid.—This preparation, which is also known as nitromuriatic acid, is not of a definite chemical composition, but is considered by physicians a valuable remedial agent. When strong nitric and hydrochloric acids are brought into contact, mutual decomposition takes place, the composition of the finished product depending upon the proportions of the acids used and the temperature at which they have been mixed. The Pharmacopœia directs 18 volumes of nitric acid and 82 volumes of hydrochloric acid, and, when so mixed, the following reactions probably take place: $HNO_3 + 3HCl = NOCl + Cl_2 + 2H_2O$ and $2HNO_3 + 6HCl = 2NOCl_2 + Cl_2 + 4H_2O$, nitrosyl mono- and dichloride and water being formed, while chlorine is liberated. The mixture is at first colorless, but as reaction progresses an orange-red color is developed and effervescence is observed; the liberated gas is very irritating, hence the operation should be conducted in a cool place, in the open air or under a flue. This preparation should never be made extemporaneously, as severe accidents may result from such a proceeding; sufficient time must be allowed for complete reaction, which is known by cessation of effervescence, after which the liquid, which has assumed a green-yellow color, should be preserved in dark, glass-stoppered bottles, in a cool place. Nitrohydrochloric acid must never be dispensed in completely filled bottles, and the patient should be cautioned against keeping it in a warm room. The acid is also known as chloro-nitrous acid and aqua regia, and owes its power of dissolving gold to the free chlorine and feeble chlorine compounds present.

Diluted Nitrohydrochloric Acid.—This solution is of nearly one-fourth the strength of the stronger acid, 22.5 per cent., and is prepared in exactly the same manner, the diluent, distilled water, not being added until effervescence has ceased. The British Pharmacopœia prepares this acid by mixing the stronger acids at once with the water and setting the mixture aside for fourteen days. Conflicting views exist regarding the composition of the finished product, some authorities contending that, when made by diluting the strong acids at once with water, the same reactions will occur as in a mixture of the acids alone, except that the decomposition is more gradual, while others assert that little or no change will take place, and that, in fact, the decomposed strong acids will be again restored to their original condition upon the addition of water, nitric and hydrochloric acids being regenerated. Certain it is that the diluted nitrohydrochloric acid differs from the strong acid in being free from color and possessing only a faint odor of chlorine when freshly made, which is gradually lost. The author has never observed any effervescence or change of color or odor upon mixing the strong acids direct with water and allowing the mixture to stand.

Phosphoric Acid.—The official acid is a dense syrupy liquid containing 85 per cent. of absolute orthophosphoric acid, H_3PO_4 or $PO(OH)_3$, and has a specific gravity of 1.707 at 25° C. (77° F.). Medicinal phosphoric acid should all be made direct from phosphorus; usually oxidation by means of nitric acid is resorted to, each part of phosphorus requiring about 3½ parts of absolute nitric acid for complete conversion, according to the following equation: $5HNO_3 + P_3 + 2H_2O = 3H_3PO_4 + 5NO$.

In order to control the reaction, about an equal weight of water is mixed with a portion of the nitric acid contained in a flask, the phosphorus is added, and the whole heated on a water-bath; when the reaction slackens, the remainder of the nitric acid is added, undiluted, small portions at a time, and the heat is continued until all the phosphorus is dissolved, after which the liquid is heated in a porcelain dish, on a sand-bath, at a temperature not exceeding 190° C. (374° F.), until all traces of nitric acid have been removed. The object of limiting the temperature is to avoid conversion of the orthophosphoric acid into pyrophosphoric acid, which occurs at 200° C. (392° F.) and over. Phosphorus is frequently contaminated with arsenic, which is best removed, at this stage of the process, by diluting the acid liquid with water, passing a stream of hydrogen sulphide through it for several hours and afterward setting the liquid aside for twenty-four hours to allow the arsenic sulphide to subside. After filtration the excess of gas is removed by heating and the liquid evaporated to the desired density, every 100 Gm. of phosphorus used yielding about 370 Gm. of official phosphoric acid. This is essentially the modified process suggested some years ago by Dr. Squibb.

In 1875, Markoe proposed the following process, which has since then been used with marked success on a large scale: 900 Gm. of phosphorus are placed in a stone jar and covered with 5400 Gm. of water, after which 10 Gm. of iodine are added and the mixture stirred so as to bring the iodine into contact with the phosphorus. From a glass-stoppered burette or funnel 60 Gm. of bromine are now added, drop by drop, in such a manner that the bromine shall strike the phosphorus as it falls below the water. Phosphorus pentaiodide and pentabromide, PI_5 and PBr_5, chiefly the latter, are formed by direct union, and when the reaction has ceased 5400 Gm. of nitric acid are added, the jar is placed in cold water or surrounded with ice, to control the rate of oxidation, and set aside until solution of the phosphorus has been effected. The acid liquid is then evaporated and treated as above. The phosphorus iodide and bromide are decomposed by the water present, forming phosphoric, hydriodic, and hydrobromic acids; the last two are decomposed by the nitric acid regenerating iodine and bromine with the liberation of nitric oxide. These reactions, continuing until all the phosphorus has been converted into phosphoric acid, may be expressed by the following equations: 1. $PI_5 + 5PBr_5 + 24H_2O = 6H_3PO_4 + 5HI + 25HBr$; 2. $HI + 5HBr + 2HNO_3 = I + 5Br + 2NO + 4H_2O$. The process can be conducted with bromine alone, but the presence of iodine has been found to modify the action between the phosphorus and bromine.

The impurities likely to be met with in phosphoric acid can, as a rule, be avoided in the process of manufacture, phosphorous acid being due to insufficient oxidation, while meta- and pyrophosphoric acids arise from the use of excessive heat.

Phosphoric acid made from phosphorus should be miscible with tincture of ferric chloride in all proportions, but, if made from glacial phosphoric acid, it causes turbidity, which is in part due to the presence of sodium metaphosphate in the glacial acid.

The value of the volumetric assay of phosphoric acid depends largely upon the indicator employed; complete neutralization is not feasible, since the normal alkali phosphate itself gives an alkaline reaction. Phosphoric acid is tribasic, and, therefore, capable of forming three different compounds with the alkalies, namely, KH_2PO_4, K_2HPO_4, and K_3PO_4; the last-named salt is alkaline to all color-indicators, whereas the other two are either acid, alkaline, or neutral to different indicators. With phenolphtalein, KH_2PO_4 shows an acid reaction, but K_2HPO_4 a neutral reaction, but with methyl-orange and congo-red, KH_2PO_4 already shows a neutral reaction, and K_2HPO_4 an alkaline reaction. Therefore, when phenolphtalein is used as an indicator, as prescribed in the Pharmacopœia, two molecules of potassium hydroxide will be required for every molecule of absolute phosphoric acid to form the salt K_2HPO_4, secondary or dipotassium phosphate, according to the equation $H_3PO_4 + 2KOH = K_2HPO_4 + 2H_2O$. Each Cc. of normal KOH solution, containing 0.05574 Gm. KOH, will indicate 0.048645 Gm. H_3PO_4, when the neutral reaction with phenolphthalein is just passed, which is shown by a permanent pink tint imparted by a drop of the alkali solution. In the official process for determining the strength of phosphoric acid 10 Gm. of the acid are diluted with water to measure 100 Cc. and of this solution 9.73 Cc. (representing 0.973 Gm. of the acid) are mixed with 10 Cc. of a cold saturated solution of sodium chloride and then titrated with normal potassium hydroxide solution each Cc. of which corresponds to 0.048645 Gm. of absolute phosphoric acid, and represents 5 per cent. of 0.973 Gm. taken; hence 17 Cc. of the alkali solution will be required to indicate 85 per cent. of absolute phosphoric acid as demanded. The object of adding saturated sodium chloride solution to the diluted acid before titration is to insure a sharp reaction and prevent hydrolysis of the potassium phosphate formed. With methyl-orange as an indicator, each Cc. of normal KOH solution represents 0.09729 Gm. H_3PO_4, for an alkaline reaction (a golden-yellow color) will be observed upon the addition of one or two drops in excess of the quantity necessary to form primary or monopotassium phosphate, KH_2PO_4, an equal number of molecules of the acid and alkali being concerned in the reaction; thus, $H_3PO_4 + KOH = KH_2PO_4 + H_2O$.

Diluted Phosphoric Acid.—It is made from the preceding acid by dilution with distilled water in the proportion of one part by weight of the strong acid and seven and one-half parts of water, or 100 Gm. and 750 Gm. It contains 10 per cent. of absolute H_3PO_4 and has a specific gravity of about 1.057 at 25° C. (77° F.).

Sulphuric Acid.—The manufacture of this acid is carried on extensively in this country and in Europe, in specially constructed leaden chambers, so arranged that the fumes from burning sulphur or iron pyrites are brought into intimate contact with steam and nitric acid vapor. Nitrogen trioxide is generated and combines with more sulphur dioxide, aqueous vapor, and atmospheric oxygen, forming nitrosylsulphuric acid, which, coming into contact with water, is decomposed, yielding sulphuric acid and nitrogen trioxide, and this, in turn, again unites with more sulphur dioxide, etc. The following equations will explain the various steps in the process:

$$\begin{aligned}
&(1)\ 2SO_2 + 2HNO_3 &&+ H_2O = 2H_2SO_4 + N_2O_3.\\
&(2)\ N_2O_3 + 2SO_2 + O_2 &&+ H_2O = 2SO_2OHNO_2.\\
&(3)\ 2SO_2OHNO_2 &&+ H_2O = 2H_2SO_4 + N_2O_3.
\end{aligned}$$

The foregoing are the chief reactions involved in the manufacture of sulphuric acid, which condenses and is dissolved in the water covering the floor of the leaden chambers, thus forming a dilute acid which gradually becomes more concentrated; it is afterward withdrawn, still further concentrated in leaden pans, and finally distilled in glass or, preferably, gold-lined platinum retorts.

Crude sulphuric acid is often colored, and contains nitric and sulphurous acids and lead, the latter being readily detected by simple dilution with water. Arsenic is almost invariably present, and thus is transferred to other substances in the manufacture of which sulphuric acid is used, as hydrochloric and nitric acids, phosphorus, etc.

When sulphuric acid is mixed with water or alcohol, heat is developed and the volume of the mixture is invariably contracted. Official sulphuric acid is of oily consistence, and has a specific gravity of 1.826 at 25° C. (77° F.). It should be free from lead and other mineral impurities, but slight traces of arsenic, nitric, nitrous, and sulphurous acids are permitted. The Pharmacopœia requires the presence of not less than 92.5 per cent. of absolute H_2SO_4, and, as sulphuric acid is bibasic, the following reaction takes place when potassium hydroxide is added to complete neutrality: $H_2SO_4 + 2KOH = K_2SO_4 + 2H_2O$. Each Cc. of normal KOH solution, containing 0.05574 Gm. KOH, is equivalent to 0.048675 Gm. H_2SO_4.

Aromatic Sulphuric Acid.—An alcoholic solution of sulphuric acid, flavored with ginger and cinnamon, containing about 11 per cent. by volume, or about 20 per cent. by weight, of official acid. It is a light-colored liquid having a specific gravity of about 0.933 at 25° C. (77° F.). The acid should be added to the alcohol slowly in a thin stream, with constant stirring, and, when the mixture has cooled, the tincture of ginger and oil of cinnamon may be added. Upon standing, chemical action ensues and a part of the sulphuric acid is gradually converted into ethyl-sulphuric or sulphovinic acid, according to the equation $H_2SO_4 + C_2H_5OH = C_2H_5HSO_4 + H_2O$. The new compound, also known as acid ethyl sulphate, is soluble in water and alcohol, but is not precipitated by barium chloride; by boiling, it is split up into sulphuric acid and alcohol; hence the Pharmacopœia directs in the official test that 10 Gm. of aromatic sulphuric acid shall be mixed with 30 Cc. of water and then boiled for a few minutes, after which sufficient water is added to bring the volume up to 100 Cc., of which 48.68 Cc., representing 4.868 Gm. of the original aromatic acid, are used for the assay. An excess, 25 Cc. of normal potassium hydroxide solution, is added and the alkaline liquid then titrated with normal sulphuric acid; not more than 5 Cc. of the latter should be used to neutralize the solution, showing that not less than 20 Cc. of the normal KOH solution were required for the 4.868 Gm. of aromatic acid taken, which would indicate not less than 20 per cent. of sulphuric acid. As each Cc. of the normal alkali solution represents 0.048675 Gm. of absolute H_2SO_4, it corresponds to 1 per cent. of 4.868 Gm.

The aromatic sulphuric acid of the present Pharmacopœia differs considerably from the preparation of the same name of the 1870 Pharmacopœia, formerly often prescribed under the name of *Elixir of Vitriol.* The latter preparation was of a brownish-red color, and very prone to precipitation; it was made by percolating 1 troy ounce of ginger and 1½ troy ounces of cinnamon with 1 pint of alcohol, and adding the resulting tincture to a previously prepared and cooled mixture of 1 pint of alcohol and 6 troy ounces of sulphuric acid.

Diluted Sulphuric Acid.—This is made by diluting 10 parts by weight of official sulphuric acid with 82½ parts of distilled water, or 100 Gm. of the former with 825 Gm. of the latter. The acid should be added gradually, with constant stirring, on account of the heat developed. It contains 10 per cent. of absolute H_2SO_4 and has a specific gravity of about 1.067 at 25° C. (77° F.).

Sulphurous Acid.—Under this name the Pharmacopœia recognizes an aqueous solution of sulphur dioxide, containing not less than 6.4 per cent. by weight of the gas. The official directions for preparing the solution are explicit, and, if followed, cannot fail to yield a satisfactory product. The charcoal acts as a deoxidizing agent upon the sulphuric acid, sulphur dioxide and carbon dioxide being generated, as shown in the following equation: $4H_2SO_4 + C_2 = 4SO_2 + 2CO_2 + 4H_2O$. Heat is necessary to induce the reaction, and in order to intercept any impurities which may be mechanically carried over with the escaping gases the latter are made to pass through water contained in a wash-bottle. The carbon dioxide will escape from the bottle containing the distilled water as the sulphur dioxide is absorbed, since it is insoluble in a solution of sulphurous acid. When the evolution of gas has ceased the solution of sulphurous acid is assayed and sufficient distilled water added to bring the product up to the strength demanded by the Pharmacopœia, 6.4 per cent. by weight of sulphur dioxide.

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CHAPTER XLI.

THE COMPOUNDS OF POTASSIUM.

THE Pharmacopœia recognizes 17 salts of potassium, besides 5 preparations of salts, including 3 liquids, for which working formulas are given; the following comprise the list:

Official English Name.	Official Latin Name.
Potassium Acetate,	Potassii Acetas.
Potassium Bicarbonate,	Potassii Bicarbonas.
Potassium Bitartrate,	Potassii Bitartras.
Potassium Bromide,	Potassii Bromidum.
Potassium Carbonate,	Potassii Carbonas.
Potassium Chlorate,	Potassii Chloras.
Potassium Citrate,	Potassii Citras.
Effervescent Potassium Citrate,	Potassii Citras Effervescens.
Potassium Cyanide,	Potassii Cyanidum.
Potassium Dichromate,	Potassii Dichromas.
Potassium and Sodium Tartrate,	Potassii et Sodii Tartras.
Potassium Ferrocyanide,	Potassii Ferrocyanidum.
Potassium Hydroxide,	Potassii Hydroxidum.
Potassium Hypophosphite,	Potassii Hypophosphis.
Potassium Iodide,	Potassii Iodidum.
Potassium Nitrate,	Potassii Nitras.
Potassium Permanganate,	Potassii Permanganas.
Potassium Sulphate,	Potassii Sulphas.
Solution of Potassium Arsenite,	Liquor Potassii Arsenitis.
Solution of Potassium Citrate,	Liquor Potassii Citratis.
Solution of Potassium Hydroxide,	Liquor Potassii Hydroxidi.
Troches of Potassium Chlorate,	Trochisci Potassii Chloratis.

Potassium Acetate. $KC_2H_3O_2$ or CH_3COOK.—This salt is prepared by neutralizing acetic acid with potassium carbonate or bicarbonate, the latter being preferable on account of its greater purity, evaporating the resulting solution to dryness, fusing the residue, and allowing the salt to solidify. The product, being very deliquescent, must be bottled while still warm, and should be well protected against air.

The salt absorbs moisture very quickly when in contact with air, which it is impossible to prevent while weighing, hence only 98 per cent. of acetate is officially demanded.

In order to determine the quality of organic salts of potassium volumetrically, it is necessary that they first be converted into carbonate by thorough ignition, the oxygen of the atmosphere aiding in the change. In the case of potassium acetate the following reaction occurs: $2KC_2H_3O_2 + O_8 = K_2CO_3 + 3H_2O + 3CO_2$, two molecules, or 194.88 parts, of acetate furnishing one moclecule, or 137.27

in the case of potassium acetate, and then titrating with half-normal acid. The following equations show that 373.56 Gm. of potassium bitartrate yield 137.27 Gm. of the carbonate, and that therefore each Cc. of $\frac{N}{2}$ H_2SO_4 must correspond to 0.09339 Gm. $KHC_4H_4O_6$: $2KHC_4H_4O_6 + O_{10} = K_2CO_3 + 7CO_2 + 5H_2O$ and $K_2CO_3 + H_2SO_4 = K_2SO_4 + CO_2 + H_2O$.

In the official test directing the use of 1 Gm. of potassium bitartrate, each Cc. of the half-normal acid required to neutralize the alkaline solution obtained will indicate 9.339 per cent. of pure bitartrate (1 Cc. of half-normal acid corresponding to 0.09339 Gm. $KHC_4H_4O_6$) and hence 10.6 Cc. will be necessary to show 98.99 (practically 99) per cent., the degree of purity demanded.

Much of the cream of tartar sold is of inferior quality and often largely adulterated, but there is no difficulty in procuring the official article if it is desired, as it is extensively manufactured in this country and abroad.

The so-called soluble cream of tartar, or borotartrate of potassium and sodium, is officially recognized in the German Pharmacopœia under the name *tartarus boraxatus.* It is soluble in its own weight of cold water, and is prepared by digesting 5 parts of potassium bitartrate in a solution of 2 parts of borax and 15 parts of water until dissolved; the solution is evaporated to dryness, and the residue, while still warm, reduced to powder.

Potassium Bromide. KBr.—This well-known salt may be obtained by decomposing a solution of ferrous bromide with potassium carbonate, heating the mixture, filtering, evaporating the filtrate, and crystallizing. The process followed by large manufacturers is to add bromine to a solution of potassium hydroxide until the liquid remains colored, evaporate it to dryness, and expose the saline residue, mixed with charcoal, in small portions at a time, to red heat in an iron crucible; the fused mass is treated with water, the resulting solution filtered, and set aside to crystallize. When bromine and potassium hydroxide are brought together, potassium bromide and bromate are formed; thus, $6KOH + Br_6 = 5KBr + KBrO_3 + 3H_2O$; by heating the mixed salts with charcoal all bromate is reduced to bromide; thus, $KBrO_3 + C_3 = KBr + 3CO$.

The chief impurity likely to be encountered in potassium bromide is the chloride, due to the chlorine present in bromine. The Pharmacopœia demands the absence of more than 3 per cent. of chloride, which is ascertained volumetrically with $\frac{N}{10}$ silver nitrate solution. Since potassium chloride has a lower molecular weight (74.04) than the bromide (118.22), an equal weight of the same will require a larger amount of silver solution for complete precipitation; upon this the official test is based.

The following rule will enable any one to ascertain the exact percentage of potassium chloride in any sample of bromide: Calculate how much $\frac{N}{10}$ $AgNO_3$ solution will be required to precipitate a given weight of pure potassium bromide, and find also the quantity necessary to precipitate the same weight of pure potassium chloride. (Assuming that 0.3 Gm. of each salt be taken, it will require 25.38 Cc. of the silver solution for the bromide, and 40.51 Cc. for the chloride.) Subtract the lesser amount from the greater (40.51—25.38 = 15.13), and the remainder will represent the difference for 100 per cent., or absolute purity. If this remainder be divided by 100 (15.13 ÷ 100 = 0.1513), the quotient will represent the quantity of $\frac{N}{10}$ $AgNO_3$ solution necessary to indicate 1 per cent. Divide the quotient so obtained into the difference between the quantity of $\frac{N}{10}$ $AgNO_3$ solution required for the given weight of a sample of bromide and for the same weight of pure bromide, the result will indicate the percentage of chloride in the sample.

When potassium chromate is used as an indicator, no permanent red color, due to silver chromate, can appear in the official test until all bromide and chloride have been precipitated. Applying the above rule to the quantities of potassium bromide and silver solution prescribed by the Pharmacopœia, 3 per cent. of chloride will be found indicated, as can be shown in the following calculations: 1 Cc. of $\frac{N}{10}$ $AgNO_3$ solution represents 0.011822 Gm. KBr or 0.007404 Gm. KCl, for 168.69 parts of silver nitrate will completely precipitate 118.22 parts of potassium bromide, or 74.04 parts of potassium chloride; therefore 0.3 Gm. KBr, if absolutely pure, will require 25.38 Cc. of $\frac{N}{10}$ $AgNO_3$ solution, for 0.3 ÷ 0.011822 = 25.38, and 0.3 Gm. KCl, if pure, requires 40.51 Cc. of $\frac{N}{10}$ $AgNO_3$ solution, for 0.3 ÷ 0.007404 = 40.51; 40.51 — 25.38 = 15.13, and 15.13 ÷ 100 = 0.1513. As the Pharmacopœia directs that not less than 24.6 Cc. and not more than 25.85 Cc. of $\frac{N}{10}$ silver nitrate solution shall be required, the difference between 25.85 and 25.38 = 0.47 Cc. is due to the presence of chloride, and this difference divided by 0.1513 would indicate 3.1 per cent. If the quantity of silver solution used falls below that theoretically required, it is due to impurities which do not react with silver nitrate or to iodide, and as the Pharmacopœia demands the absence of iodide, the lower limit allowed in the test, 24.6 Cc., would indicate only 96.94 per cent. of pure bromide, for 24.6 × 0.011822 = 0.2908212 and 0.2908212 ÷ 0.3 = 96.94.

Potassium Carbonate. **K_2CO_3**.—This compound is familiarly known as salt of tartar, a name given to it because it was at one time prepared by ignition of tartar. It is now extensively prepared from potassium chloride by a method analogous to the Leblanc process for making sodium carbonate. The purer carbonate, such as is demanded by the Pharmacopœia, is obtained by heating crystallized potassium bicarbonate to redness, whereby carbon dioxide and water are eliminated and potassium carbonate remains, the yield being about 68 or 69 per cent. The reaction is a very simple one, $2KHCO_3 = K_2CO_3 + CO_2 + H_2O$.

Potassium carbonate, on account of its very deliquescent nature, must be preserved in well-stoppered bottles, in a dry place. The Pharmacopœia demands an almost absolutely pure salt, 98 per cent. of absolute K_2CO_3 for the salt when thoroughly dried. 1 Gm. of potassium carbonate dried at 130° C. (266° F.) should require for neutralization not less than 14.3 (14.28) Cc. of normal H_2SO_4, each Cc. corresponding to 0.068635 Gm. of K_2CO_3, and 0.98 (98 per cent. of 1) Gm. $\div$ 0.068635 $=$ 14.28.

Potassium Chlorate. $KClO_3$.—At present potassium chlorate is largely made by a process similar to that given in the British Pharmacopœia, which consists in passing chlorine gas into water holding lime, or preferably magnesia, in suspension, by which means chloride and hypochlorite of the respective metals are formed. The latter salt is decomposed by heat into chlorate and chloride, and upon treating the solution with potassium chloride a reaction sets in, by which potassium chlorate and calcium or magnesium chloride are formed, the latter salts remaining in solution, while the potassium chlorate crystallizes out. Magnesia is preferred to lime, as potassium chlorate is less soluble in solution of magnesium chloride than of calcium chloride. The reactions involved may be expressed as follows: $2Ca(OH)_2 + Cl_4 = Ca(ClO)_2 + CaCl_2 + 2H_2O$; $3Ca(ClO)_2 = Ca(ClO_3)_2 + 2CaCl_2$; $Ca(ClO_3)_2 + 2KCl = 2KClO_3 + CaCl_2$.

Large quantities of the salt are produced both in this country and in Europe by a process which consists in passing an electric current through a heated solution of potassium chloride, whereby chlorine collects around one pole (the positive) and potassium hydroxide around the other. The solution of potassium hydroxide by a process of circulation is carried to the compartment of the next cell containing the positive pole, and so on, by which it comes in contact with chlorine and forms potassium chlorate, which continually crystallizes out. The change is most simply expressed thus: $2Cl + H_2O = 2HCl + O$; $KOH + HCl = KCl + H_2O$; $KCl + O_3 = KClO_3$.

The salt is rarely found impure, and occurs in commerce both in the form of crystals and fine powder. It is readily decomposed, often with explosive violence, when triturated with such substances as sugar, tannin, sulphur, etc.; care is therefore necessary when such mixtures are to be dispensed.

Potassium Citrate. $K_3C_6H_5O_7 + H_2O$ or $C_3H_4OH(COOK)_3.H_2O$.—This salt is prepared by neutralizing a solution of citric acid with potassium carbonate or bicarbonate, and evaporating the solution to dryness, with constant stirring, so as to obtain the salt in small granules. The finished product retains a little over 5½ per cent. of water, which it loses entirely when heated to 200° C. (392° F.), but should be free from impurities; the commercial article is frequently acid, showing imperfect saturation. As the salt is deliquescent, it must be well protected against air.

In order to determine the quality of potassium citrate volumetrically, it is necessary to convert the salt into carbonate by ignition, and then to titrate with $\frac{N}{2}$ acid, as in the case of other organic potassium salts. Citric acid being tribasic, 2 molecules, or 644.16 parts, of potassium citrate will yield 3 molecules, or 411.81 parts, of carbonate; thus, $2K_3C_6H_5O_7.H_2O + O_{18} = 3K_2CO_3 + 9CO_2 + 7H_2O$; hence 1 Gm. of the salt converted into carbonate and dissolved in water will require not less than 18.4 Cc. of $\frac{N}{2}$ acid to show the degree of purity demanded by the Pharmacopœia, or 99 per cent. Each Cc. of $\frac{N}{2}$ acid corresponds to 0.05368 Gm. of $K_3C_6H_5O_7 + H_2O$, containing 5.55 per cent. of water of crystallization, and $0.99 \div 0.5368 = 18.44$.

Effervescent Potassium Citrate.—This preparation contains about 20 per cent. of potassium citrate and has already been considered on page 410 in the chapter on Granular Effervescent Salts.

Potassium Cyanide. KCN or KCy.—This very poisonous compound is prepared on a large scale by fusing together anhydrous potassium ferrocyanide with metallic potassium, with entire exclusion of air. A very pure article is produced, according to the following equation, $K_4Fe(CN)_6 + K_2 = 6KCN + Fe$; the molten saline mass is poured off, leaving metallic iron behind. For commercial purposes a mixed cyanide of potassium and sodium is produced by the same method, except that in place of metallic potassium the less expensive metallic sodium is used.

Another method for obtaining a pure salt consists in passing hydrocyanic acid gas into an alcoholic solution of potassium hydroxide, when the newly formed cyanide will separate as a bulky crystalline precipitate, which may be washed on a filter with alcohol.

The Pharmacopœia demands not less than 95 per cent. of pure KCN, which is determined volumetrically by means of $\frac{N}{10}$ $AgNO_3$ solution in the presence of ammonia water, potassium iodide being used as an indicator. As potassium cyanide forms with silver nitrate a soluble double cyanide of potassium and silver, as shown by the equation $2KCN + AgNO_3 = AgK(CN)_2 + KNO_3$, no precipitate will appear until one-half of the potassium cyanide has been acted upon by silver nitrate, after which the solution becomes cloudy by precipitation of silver iodide insoluble in the ammonia water. From the above equation it follows that 1 molecule or 168.69 Gm. of silver nitrate reacts with 2 molecules or 129.4 Gm. of potassium cyanide, and that in the official test each Cc. of $\frac{N}{10}$ $AgNO_3$ solution will correspond to 0.01294 Gm. of pure KCN, which is exactly 2 per cent. of the 0.647 Gm. of the alkali cyanide taken; hence 47.5 Cc. of the silver solution will be required before appearance of a permanent precipitate, showing the presence of 95 per cent. of pure KCN, as demanded. Sodium cyanide is frequently found in potassium cyanide, and since the Pharmacopœia does not distinguish in the test between cyanides of potassium and sodium, the titration method does not give the exact amount of KCN, but it does indicate the true amount of hydrocyanic acid in combination. The official potassium cyanide contains 39.4 per cent. of hydrocyanic acid, and as far as efficiency is concerned it is immaterial whether the salt contains sodium cyanide or not, since a mixed cyanide containing 39.4 per cent. of HCN is equivalent to potassium cyanide 95 per cent. pure. The number of Cc. of $\frac{N}{10}$ $AgNO_3$ solution used in the above test multiplied by 0.00537 indicates the quantity of hydrocyanic acid in combination, and $47.5 \times 0.00537 = 0.255$, which is practically identical with 0.253 or 39.4 per cent. of 0.647.

Potassium Dichromate. $K_2Cr_2O_7$.—This salt, commercially generally called bichromate of potash, is not used medicinally, but is of considerable interest in analytical chemistry and is largely used in the arts. It may be looked upon as a salt of dichromic acid, which latter is the result of the union of 2 molecules of chromic acid, with the elimination of water; thus: $H_2CrO_4 + H_2CrO_4 = H_2Cr_2O_7 + H_2O$, or it may be assumed that chromium trioxide is capable of forming both chromic and dichromic acid; thus: $CrO_3 + H_2O = H_2CrO_4$ and $2CrO_3 + H_2O = H_2Cr_2O_7$. Dichromic acid may be said to be chromic acid holding chromic trioxide in solution, and is analogous to disulphuric, or fuming sulphuric, acid.

Potassium dichromate is obtained by treating a solution of the chromate with sulphuric acid—thus, $2K_2CrO_4 + H_2SO_4 = K_2Cr_2O_7 + K_2SO_4 + H_2O$—and separating the resulting salts by crystallization. The chromate is obtained direct from chrome-iron ore, $FeOCr_2O_3$, by roasting the same, in reverberatory furnaces, with potassium carbonate and chalk, the latter simply preventing fusion of the mixture, which is finally treated with water and strained to remove the iron.

Potassium and Sodium Tartrate. $KNaC_4H_4O_6 + 4H_2O$ or $(CHOH)_2COONaCOOK + 4H_2O$.—This salt is commercially known as Rochelle Salt from the fact that it was first obtained at Rochelle, France, by an apothecary named Seignette, more than two hundred years ago. It is prepared by neutralizing the free acid in cream of tartar with sodium carbonate, whereby a normal double tartrate is produced; the solution, which must be neutral, is boiled for a short time, filtered, concentrated, and set aside to crystallize, the crystals being afterward pulverized. According to the following equation, $2KHC_4H_4O_6 + (Na_2CO_3 + 10H_2O) = 2(KNaC_4H_4O_6.4H_2O) + CO_2 + 3H_2O$, 8 parts of official cream of tartar will require about 6 parts of crystallized pure sodium carbonate, yielding about 12 parts of crystallized Rochelle Salt.

Potassium and sodium tartrate is recognized in the British Pharmacopœia by the name of *soda tartarata,* and in the German Pharmacopœia as *tartarus natronatus;* it is also known as *sal Seignetti.*

The Pharmacopœia requires that the salt shall contain not less than 99 per cent. of pure $KNaC_4H_4O_6$, which may be determined by converting it into carbonate and then titrating with $\frac{N}{2}$ acid. The equation $KNaC_4H_4O_6.4H_2O + O_5 = KNaCO_3 + 3CO_2 + 6H_2O$ shows that 280.18 Gm. of the double tartrate will yield 121.29 Gm. of the double carbonate, which are capable of neutralizing 4,000 Cc. of $\frac{N}{2}$ acid; hence each Cc. of the latter corresponds to 0.070045 Gm. of potassium and sodium tartrate, and 14.14 Cc. will be required in the official test to indicate 99 per cent. purity.

Potassium Ferrocyanide. $K_4Fe(CN)_6 + 3H_2O$.—Yellow prussiate of potash, as it is commercially called, possesses no medicinal properties, but is used for making hydrocyanic acid and other cyanides; when pure the salt is not poisonous. It is made by heating, in iron vessels, with constant stirring, a mixture of potassium carbonate, metallic iron, and scraps of horn, leather, or other nitrogen-containing substances. The fused mass, known as "melt," is, after cooling, leached with water, and the solution decanted and crystallized; the insoluble residue consists of iron, charcoal, ferrous sulphide, calcium phosphate, and silica.

When chlorine is passed into a solution of potassium ferrocyanide the ferricyanide, or red prussiate of potash, a valuable chemical reagent, is produced, as shown by the following equation, $2K_4Fe(CN)_6 + Cl_2 = K_6Fe_2(CN)_{12}$ or $2K_3Fe(CN)_6 + 2KCl$.

Potassium Hydroxide. KOH.—This compound, better known as caustic potash, is obtained by decomposing a solution of potassium carbonate with milk of lime, evaporating the clear filtrate in perfectly clean iron or silver vessels until a small quantity of the liquid congeals upon cooling, and then pouring it into cylindrical moulds, whence the sticks are removed while still warm.

The purity of the product obtained depends upon the quality of the potassium carbonate employed, and if made from the bicarbonate it is of much better quality. White caustic potash in sticks, labelled potassa by lime, is the kind generally used for pharmaceutical purposes, and should contain not over 5 or 6 per cent. of moisture; commercial caustic potash is sometimes found to contain as much as 15 or 20 per cent. of water. For chemical purposes potassium hydroxide is purified by means of alcohol or baryta, being then known as potassa by alcohol or potassa by baryta. The purest potassium hydroxide is obtained by adding pure metallic potassium in small pieces to distilled water in a silver dish and evaporating the solution.

Potassium hydroxide is a powerful caustic, very deliquescent, and rapidly absorbs carbon dioxide from the air; it must therefore be handled carefully and preserved in tightly stoppered bottles. It is soluble in less than one-half its own weight of water and in twice its weight of alcohol.

The Pharmacopœia requires that official potassium hydroxide shall contain at least 85 per cent. of absolute KOH, and not more than 2 per cent. of foreign inorganic substances other than water. Its purity is ascertained by titration with normal sulphuric acid, each Cc. of which is capable of neutralizing 0.05574 Gm. of pure potassium hydroxide. The official assay method gives absolutely accurate results only in the absence of sodium hydroxide, since the latter, having a lower molecular weight, requires a relatively larger quantity of acid for neutralization.

With a few exceptions, the limits of impurities allowed by the Pharmacopœia, in this and other compounds of potassium, rarely exceed 0.5 per cent., and are usually determined volumetrically. Since potassium hydroxide readily absorbs carbon dioxide, the Pharmacopœia limits the amount of carbonate present by directing that 10 Cc. of a 10 per cent. solution of the hydroxide shall not cause distinct effervescence if diluted sulphuric acid be added in excess.

Potassium Hypophosphite. KH_2PO_2.—Although this salt can be made by boiling phosphorus with solution of potassium hydroxide, it is preferably obtained by adding potassium carbonate to a solution of calcium hypophosphite, when calcium carbonate will be precipitated and potassium hypophosphite remain in solution, which can be recovered by filtering the mixture and carefully evaporating the filtrate on a water-bath, with constant stirring, until a granular salt results. The following equation shows the decomposition: $Ca(H_2PO_2)_2 + K_2CO_3 = 2KH_2PO_2 + CaCO_3$.

Potassium hypophosphite is very deliquescent, and must be preserved in tightly stoppered bottles; as it readily explodes when intimately mixed with oxidizing agents, trituration with such substances must be avoided.

The official salt is required to contain at least 98 per cent. of pure KH_2PO_2, which can be determined accurately only by gravimetric estimation in the usual manner as magnesium pyrophosphate, after removal of phosphite by means of lead acetate and oxidation of the hypophosphite to phosphate by means of bromine. The volumetric method of determining hypophosphites by means of potassium permanganate, formerly official, has been shown to be unreliable owing to the almost invariable presence of phosphites.

Potassium Iodide. KI.—When iodine is added to a solution of potassium hydroxide the two substances combine, forming potassium iodide and iodate; thus, $6KOH + I_6 = 5KI + KIO_3 + 3H_2O$. The process of manufacturing this salt is analogous to that given for potassium bromide, the iodate being reduced to iodide by heating with charcoal.

Much of the commerical potassium iodide does not respond to the requirements of the Pharmacopœia, as it occurs in white, opaque crystals, which, having been obtained from an alkaline solution, are less pure; the official requirements demand practically total absence of alkali, and such a salt crystallizes in colorless, transparent cubes, but can also be obtained in the form of a white granular powder. The pharmacopœial test for the presence of potassium cyanide (due to cyanogen derived from the iodine) involves the formation of potassium ferrocyanide, which, reacting with ferrous sulphate, rapidly produces a blue color, owing to the oxidizing effect of the air. Since each Cc. of $\frac{N}{10}$ $AgNO_3$ solution represents 0.016476 Gm. KI, 0.5 Gm. of an absolutely pure salt will require 30.35 Cc. for complete precipitation; if more than this quantity be required, it would indicate the presence of bromide or chloride. The Pharmacopœia requires at least 99 per cent. of pure iodide, and hence states that 0.5 Gm. shall require not less than 30 nor more than 30.8 Cc. of $\frac{N}{10}$ $AgNO_3$ solution for complete precipitation of the salt, potassium chromate being used as an indicator. As each 0.3728 Cc. of the silver solution consumed in excess of the theoretical quantity necessary for pure iodide indicates 1 per cent. of chloride, assuming this to be the impurity present, the excess of 0.45 (30.8—30.35) Cc. allowed by the Pharmacopœia would indicate 1.2 per cent. of potassium chloride. The lower limit allowed, 30 Cc., is less than the theoretical quantity required and may be due to impurities having no action on the silver solution; as each Cc. of $\frac{N}{10}$ $AgNO_3$ solution corresponds to 0.016476 Gm. of pure potassium iodide the 30 Cc. would indicate 0.49428 Gm. or 98.85 per cent. of the 0.5 Gm. used in the test.

Potassium Nitrate. **KNO_3.**—The sources of this salt were at one time chiefly the natural deposits in India and extensive plantations in Europe and elsewhere for the artificial production of potassium nitrate by putrefaction of animal and vegetable matter in the presence of wood-ashes and calcareous earth. It is now largely obtained by mutual decomposition of potassium chloride and native sodium nitrate, advantage being taken of the lesser solubility of the newly formed sodium chloride in hot water to rid the solution of this impurity upon concentration by boiling. The potassium nitrate subsequently crystallizes out, and is further purified by re-solution and re-crystallization.

Potassium nitrate is to be had both in the form of large crystals and as a fine granular powder; the latter is preferred for pharmaceutical purposes, and is largely obtained from manufacturers of gunpowder, who require a pure article for their purposes.

The name saltpetre, or nitre, is used almost exclusively in commerce for this salt, and when fused and cast into round moulds it is sold under the name *sal prunelle.*

Potassium Permanganate. **$KMnO_4$.**—In the manufacture of this compound the first step necessary is the production of potassium manganate, by heating to semi-fusion at a dull-red heat, an intimate mixture of manganese dioxide, potassium hydroxide, and potassium chlorate, when the following reaction occurs: $3MnO_2 + 6KOH + KClO_3 = 3K_2MnO_4 + KCl + 3H_2O$. The green fused mass is then treated twice with boiling water, whereby the potassium manganate is converted into permanganate—$3K_2MnO_4 + 2H_2O = 2KMnO_4 + MnO_2 + 4KOH$—manganese dioxide being again precipitated and potassium hydroxide remaining in solution with the permanganate. The presence of potassium hydroxide in the liquid prevents a full yield of permanganate by holding a portion of the manganate in solution without change; a stream of carbon dioxide is therefore passed into the liquid to neutralize the alkali and thus allow all the manganate to be converted into permanganate and dioxide; in place of carbon dioxide, diluted sulphuric acid is sometimes used for the same purpose. Finally, after decantation and filtration through asbestos, the solution is concentrated and set aside to crystallize. As potassium permanganate is readily decomposed by organic matter, all dust and dirt must be excluded during the last steps of the process.

The official method of valuation of potassium permanganate by means of oxalic acid depends upon the ready deoxidation of the salt by all reducing substances, five atoms of oxygen being liberated from every two molecules of the permanganate. In the official test the oxalic acid is completely converted by oxidation into carbon dioxide and water, as shown by the following equation: $5(H_2C_2O_4 + 2H_2O) + 2KMnO_4 + 3H_2SO_4 = 10CO_2 + K_2SO_4 + 2MnSO_4 + 18H_2O$, 625.5 parts of crystallized oxalic acid requiring 313.96 parts of pure permanganate. The Pharmacopœia demands potassium permanganate to be of 99 per cent. purity, and hence 0.1 Gm. of the salt (0.099 Gm. of pure $KMnO_4$) will oxidize 0.19724 Gm. of crystallized oxalic acid, or in other words, 0.19724 Gm. of the oxalic acid will be required to discharge the color of a solution containing 0.1 Gm. of official potassium permanganate. Such a quantity of the acid is contained in 31.52 Cc. of $\frac{N}{10}$ solution, as each Cc. contains 0.006255 Gm. and $0.19724 \div 0.006255 = 31.517+$. If 31.5 Cc. of $\frac{N}{10}$ oxalic acid solution be used, as stated in the Pharmacopœia, this would indicate the presence of 0.09889 Gm. of pure $KMnO_4$ or 98.89 per cent., which is practically 99 per cent., as demanded.

Since potassium permanganate is easily decomposed, it should never be triturated or dispensed with readily oxidizable or organic substances. Stains produced by the salt in a mortar or on the hands are best removed with oxalic acid solution, either alone or with a little sulphuric acid.

While potassium permanganate is used to some extent in medicine, it is of special interest to pharmacists as an oxidizing agent in volumetric analysis.

Potassium Sulphate. **K_2SO_4.**—This salt, which, although rarely used in medicine or pharmacy, has been retained in the Pharmacopœia, is obtained partly as a by-product in many chemical operations and partly from the mineral kainite, a natural potassium and magnesium sulphate.

For a long time potassium sulphate, on account of the hardness of its crystals, was preferred as a diluent in the preparation of Dover's Powder, and is to-day used by some for this purpose.

Solution of Potassium Arsenite.—This preparation can be more conveniently studied in connection with the preparations of arsenic.

Solution of Potassium Citrate.—The Pharmacopœia very properly directs the extemporaneous preparation of this solution, as it does not keep well and soon loses its refreshing taste. The proportions of citric acid, 6 Gm., and potassium bicarbonate, 8 Gm., in the official formula show a slight excess of citric acid over the quantity necessary to form a neutral salt, which improves the flavor of the finished product. The solution contains 8.55 Gm. of potassium citrate and 0.43 Gm. of citric acid in 100 Cc., besides some carbonic acid, which corresponds to about 38 grains of the salt in each fluidounce.

Although the name *mistura potassii citratis* is sometimes applied to this solution, the latter differs from the preparation formerly recognized by that name and more familiarly known as *neutral mixture*. The former preparation was made by neutralizing fresh lemon-juice, strained through cotton, with potassium bicarbonate, and possessed, therefore, a more agreeable flavor, although of uncertain strength. Some physicians still prefer the old *neutral mixture* to the present official solution in many cases.

Solution of Potassium Hydroxide.—The official Liquor Potassii Hydroxidi can be made either by decomposition of a solution of pure potassium carbonate, obtained by heating the bicarbonate with milk of lime or by simple solution of 60 Gm. of potassium hydroxide in 940 Gm. of distilled water, the latter being generally preferred by pharmacists as a matter of convenience, while the former is followed by manufacturing chemists for economical reasons. If simple solution of the potassium hydroxide be employed, it is important that the percentage of KOH present be known, in order to insure a 5 per cent. solution; the above proportions are calculated for 85 per cent. potassium hydroxide, and the proper quantity of a higher or lower grade can be readily found by the directions given in the Pharmacopœia, namely, to divide 5100 by the percentage of potassium hydroxide contained in the sample. This is arrived at as follows: the official 5 per cent. solution requires 50 Gm. of absolute or 100 per cent. KOH for 1000 Gm. of finished product, but a larger quantity of a poorer sample or a smaller quantity of a richer sample than the official potassium hydroxide will be required. In other words, the quantity of potassium hydroxide necessary will be in inverse proportion to the percentage of KOH present. Knowing that 60 Gm. of 85 per cent. potassium hydroxide are required, and representing the unknown percentage strength by p and the unknown quantity by x, we may say $p\% : 85\% :: 60 : x$, from which we derive $x = \frac{85 \times 60}{p}$, or $\frac{5100}{p}$. Thus, if the potassium hydroxide contains only 80 per cent. of KOH, it will require 63.75 ($5100 \div 80$) Gm. of potassium hydroxide and 936.25 Gm. of distilled water, for 63.75 at 80 per cent. is equal to 60 at 85 per cent., 51 being the result in both cases and yielding practically 1000 Gm. of a 5 per cent. solution.

The object, in the first process, of heating the bicarbonate in solution until effervescence ceases, is to convert it into monocarbonate, and thus obtain a purer article than if commercial potassium carbonate were used. By mixing the two liquids hot, and boiling the mixture for ten minutes, a more compact precipitate of calcium carbonate is produced, which settles rapidly and from which the solution of potassium hydroxide can be more readily separated.

The process involves two simple reactions: 1. $2KHCO_3 = K_2CO_3 + CO_2 + H_2O$; 2. $K_2CO_3 + Ca(OH)_2 = 2KOH + CaCO_3$. Lime is used in excess of the theoretical requirement on account of its slight solubility, and experience has also taught that considerable dilution of the two liquids is necessary, as the reaction cannot be completed in concentrated solutions.

In order to preserve the quality of the solution of potassium hydroxide it is essential that it be kept in securely stoppered bottles, to avoid absorption of carbon dioxide; the bottles should be made of green glass, as flintware is easily acted upon, and the stoppers should be thinly coated with paraffin or petrolatum, to prevent their becoming "fixed." Solution of potassium hydroxide should never be filtered through paper, which is rapidly attacked by the alkali; large volumes are best decanted or siphoned from any sediment, while small quantities may be conveniently filtered through glass-wool or asbestos.

The official solution of potassium hydroxide has a specific gravity of about 1.046 at 25° C. (77° F.), and should contain about 5 per cent. of potassium hydroxide, which is equal to about 27 grains in each fluidounce; its strength is determined volumetrically with normal acid, each Cc. of which corresponds to 0.05574 Gm. KOH.

Besides the potassium salts officially recognized, the following are occasionally used in medicine and pharmacy:

Potassium Benzoate. $KC_7H_5O_2 + 3H_2O$ **or** $C_6H_5COOK.3H_2O$.—This salt can be most conveniently obtained by adding benzoic acid to a solution of potassium bicarbonate and evaporating the resulting solution; 100 parts of benzoic acid require 82.9 parts of potassium bicarbonate for complete neutralization, yielding 175.5 parts of a salt having the above composition.

Potassium Chloride. **KCl.**—This may be obtained as a by-product in the manufacture of other salts, but is chiefly derived from the mineral carnallite, a double potassium and magnesium chloride, extensively mined in Germany.

Potassium Salicylate. **$2KC_7H_5O_3 + H_2O$ or $2(C_6H_4(OH)COOK).H_2O$.**—This can be readily prepared in the manner outlined for potassium benzoate, simply using salicylic acid in place of benzoic acid, 100 parts of the former requiring 73.29 parts of potassium bicarbonate and yielding 127.6 parts of the newly formed salt.

Potassium Sulphite. **$K_2SO_3 + 2H_2O$.**—When sulphur dioxide is passed into a solution of potassium carbonate until the carbon dioxide has all been expelled, and another portion of potassium carbonate equal in weight to that first used is then added, potassium sulphite will crystallize on concentration of the solution. If, in place of more potassium carbonate, strong alcohol be added to the solution containing sulphur dioxide in excess, potassium bisulphite, $KHSO_3$, will crystallize out.

Potassium Tartrate. **$K_2C_4H_4O_6 + H_2O$ or $(CHOH)_2(COOK)_2.H_2O$.**—Normal potassium tartrate is made from the bitartrate by neutralizing the excess of acid present with potassium carbonate. The salt is not official in the U. S. Pharmacopœia, but is still recognized in the British and German Pharmacopœias.

CHAPTER XLII.

THE COMPOUNDS OF SODIUM.

THE official salts of sodium resemble those of potassium in many respects and are frequently prepared by analogous processes. Twenty five salts, besides 3 liquid and 2 solid preparations, are recognized in the Pharmacopœia, as follows:

Official English Name.	Official Latin Name.
Sodium Acetate,	Sodii Acetas.
Sodium Arsenate,	Sodii Arsenas.
Exsiccated Sodium Arsenate,	Sodii Arsenas Exsiccatus.
Sodium Benzoate,	Sodii Benzoas.
Sodium Bicarbonate,	Sodii Bicarbonas.
Sodium Bisulphite,	Sodii Bisulphis.
Sodium Borate,	Sodii Boras.
Sodium Bromide,	Sodii Bromidum.
Sodium Carbonate, Monohydrated,	Sodii Carbonas Monohydratus.
Sodium Chlorate,	Sodii Chloras.
Sodium Chloride,	Sodii Chloridum.
Sodium Citrate,	Sodii Citras.
Sodium Hydroxide,	Sodii Hydroxidum.
Sodium Hypophosphite,	Sodii Hypophosphis.
Sodium Iodide,	Sodii Iodidum.
Sodium Nitrate,	Sodii Nitras.
Sodium Nitrite.	Sodii Nitris.
Sodium Phenolsulphonate,	Sodii Phenolsulphonas.
Sodium Phosphate,	Sodii Phosphas.
Effervescent Sodium Phosphate,	Sodii Phosphas Effervescens.
Exsiccated Sodium Phosphate,	Sodii Phosphas Exsiccatus.
Sodium Pyrophosphate,	Sodii Pyrophosphas.
Sodium Salicylate,	Sodii Salicylas.
Sodium Sulphate,	Sodii Sulphas.
Sodium Sulphite,	Sodii Sulphis.
Sodium Thiosulphate.	Sodii Thiosulphas.
Solution of Chlorinated Soda,	Liquor Sodæ Chlorinatæ.
Solution of Sodium Arsenate,	Liquor Sodii Arsenatis.
Solution of Sodium Hydroxide,	Liquor Sodii Hydroxidi.
Troches of Sodium Bicarbonate,	Trochisci Sodii Bicarbonatis.

Sodium Acetate. $NaC_2H_3O_2 + 3H_3O$ or $CH_3COONa.3H_2O$.—This salt may be prepared by neutralizing acetic acid with sodium carbonate or bicarbonate, concentrating the resulting solution and crystallizing; in a crude form it is extensively obtained in the manufacture of acetic acid, and may be purified by roasting and other processes. Sodium acetate differs from potassium acetate in containing nearly 40 per cent. of water of crystallization, and in its stability upon exposure to air; hence less care is necessary in its preservation; it is about one-third as soluble in water and far less soluble in alcohol than the potassium salt.

The valuation of the so-called organic sodium salts is performed, as in the case of the corresponding potassium salts, by conversion into carbonate and subsequent titration with acid. The following equation, $2(NaC_2H_3O_2 + 3H_2O) + O_8 = Na_2CO_3 + 3CO_2 + 9H_2O$, shows that two molecules, or 270.2 parts, of crystallized sodium acetate yield, upon complete ignition, one molecule, or 105.31 parts, of anhydrous sodium carbonate; hence each Cc. of $\frac{N}{2}$ H_2SO_4, neutralizing 0.026327 Gm. Na_2CO_3, corresponds to 0.06755 Gm. $NaC_2H_3O_2 + 3H_2O$. The Pharmacopœia demands that the official sodium acetate shall be 99.5 per cent. pure, and 1.0 Gm. of the salt must, therefore, after complete ignition require 14.74 Cc. of $\frac{N}{2}$ acid to neutralize the alkaline residue, as stated in the official test.

Sodium Arsenate. $Na_2HAsO_4 + 7H_2O$.—The official salt, as shown by the chemical formula, is disodium orthoarsenate, and bears a close analogy to the official sodium phosphate; the exact composition must depend upon the proportions of the ingredients used in its manufacture. Sodium arsenate is usually obtained by fusing together, at a red heat, arsenic trioxide, dried sodium carbonate, and sodium nitrate; effervescence ensues, and, when complete quiet fusion has set in, the residue will consist of sodium pyroarsenate, as shown by the following equation: $As_2O_3 + 2NaNO_3 + Na_2CO_3 = Na_4As_2O_7 + N_2O_3 + CO_2$. The fused mass, having been poured on a stone slab and allowed to solidify, is dissolved, while still warm, in water, whereby the sodium pyroarsenate is converted into orthoarsenate by the appropriation of water; thus, $Na_4As_2O_7 + H_2O = 2Na_2HAsO_4$. The solution is set aside to crystallize, when a salt containing 40.4 per cent. of water, and having the above formula, will be obtained.

In the British Pharmacopœia the title Sodii Arsenas is applied to the anhydrous salt, described below.

The official salt, upon exposure to dry air, gradually loses a portion of its water of crystallization until a salt of the composition $Na_2HAsO_4 + 2H_2O$ remains, containing only 16.2 per cent. of water; hence, it should be preserved in tightly stoppered bottles.

Exsiccated Sodium Arsenate. Na_2HAsO_4.—This salt, also known as anhydrous sodium arsenate, is prepared by allowing the crystallized salt to effloresce at a temperature between 40° and 50° C. (104° and 122° F.) until completely disintegrated; the temperature is then gradually increased to 150° C. (302° F.) and continued until the product ceases to lose weight. It is then reduced to a fine powder. The object of first allowing the crystals to effloresce at a moderate temperature is to prevent fusion of the salt in its own water of crystallization, as the latter would be much more difficult to drive off in that condition. Each Gm. of the exsiccated salt corresponds to 1.677+ Gm. of the crystallized salt, but in all other respects the two salts are identical.

The reason for directing the use of exsiccated sodium arsenate in pharmacopœial preparations is to insure uniformity in the arsenic content, since the crystallized sodium arsenate may contain variable proportions of water, depending upon the temperature at which the crystals have been formed and the care with which they have been preserved.

Sodium Benzoate. $NaC_7H_5O_2$ or C_6H_5COONa.—This salt may be conveniently prepared by suspending benzoic acid in hot water and slowly adding sufficient sodium bicarbonate to form a neutral solution, which is then filtered and evaporated, with frequent stirring, on a water-bath, to dryness. 100 parts of benzoic acid require about 70 parts of official sodium bicarbonate and yield about 118 parts of sodium benzoate. The salt can also be obtained in crystalline form, having the composition $NaC_7H_5O_2 + H_2O$; but, as it effloresces readily, the Pharmacopœia has recognized only the anhydrous salt.

The valuation of sodium benzoate is made, like that of the acetate, by ignition and titration of the resulting sodium carbonate with normal acid. The equation $2NaC_7H_5O_2 + O_{30} = Na_2CO_3 + 5H_2O + 13CO_2$ shows that 286.02 parts of sodium benzoate will yield 105.31 parts of anhydrous sodium carbonate; therefore each Cc. $\frac{N}{2}$ H_2SO_4 represents 0.071505 Gm. $NaC_7H_5O_2$. Using 1 Gm. of the salt, as directed in the official test, 13.85 Cc. $\frac{N}{2}$ H_2SO_4 will be required to neutralize the alkaline residue if 99 per cent. $NaC_7H_5O_2$ be present, for 99 per cent. of $1 = 0.99$ and $0.99 \div 0.071505 = 13.84+$.

Sodium Bicarbonate. $NaHCO_3$.—This well-known compound is manufactured on a large scale by different processes. If sodium carbonate in crystalline form be treated with carbon dioxide, anhydrous sodium bicarbonate, or acid carbonate, will be formed and water eliminated; thus, $(Na_2CO_3 + 10H_2O) + CO_2 = 2NaHCO_3 + 9H_2O$; by using a mixture of anhydrous and crystallized sodium carbonate, a part of the eliminated water will be required for converting the former into bicarbonate, the rest being allowed to escape by drainage. Sodium bicarbonate is obtained also as an intermediate product in the manufacture of the normal carbonate by the Solvay ammonia-soda process, wherein concentrated solution of sodium chloride is mixed with ammonia and then saturated with carbon dioxide under pressure. Sodium bicarbonate is precipitated and ammonium chloride remains in solution. In either case the newly formed sodium bicarbonate is washed with small quantities of water for the purpose of removing the more soluble impurities.

The product of the Solvay process requires careful purification, owing to contamination with ammonium salts, especially ammonium carbonate; hence sodium bicarbonate, prepared from normal carbonate, is preferred for medicinal purposes.

Commercial sodium bicarbonate is frequently contaminated with carbonate and chloride; but if a pure salt is wanted, this may be readily obtained by percolating the commercial article with cold distilled water and drying the purified residue with moderate heat only.

The Pharmacopœia does not require absolute purity for sodium bicarbonate, traces of carbonate, chloride, sulphate, and sulphite being permitted. The official salt must, however, contain at least 99 per cent. $NaHCO_3$, as indicated by the demand that 2 Gm. of the salt shall require not less than 23.74 Cc. of normal H_2SO_4 for complete neutralization, each Cc. representing 0.08343 Gm. $NaHCO_3$.

Sodium Bisulphite. $NaHSO_3$.—This salt, known also as acid sodium sulphite, is rarely used in medicine. It is prepared by passing sulphur dioxide into a solution of sodium carbonate to saturation and until all carbon dioxide has been expelled, the reaction being as follows: $Na_2CO_3 + H_2O + 2SO_2 = 2NaHSO_3 + CO_2$. This solution is then concentrated and allowed to crystallize.

Sodium bisulphite is not a very stable compound, and upon exposure to air is gradually oxidized and converted into sulphate, sulphur dioxide being given off at the same time. The turbidity caused in a solution of the salt by addition of hydrochloric acid, indicating the presence of thiosulphate, is due to finely precipitated sulphur.

The Pharmacopœia demands at least 90 per cent. of absolute $NaHSO_3$ in the official compound, which is determined volumetrically by means of iodine, the latter acting as an oxidizing agent, converting the acid sulphite into an acid sulphate; thus, $NaHSO_3 + I_2 + H_2O = NaHSO_4 + 2HI$. Since 103.35 parts of the acid sulphite require 251.8 parts of iodine for complete oxidation, each Cc. $\frac{N}{10}$ I solution containing 0.01259 Gm. of iodine is capable of oxidizing 0.0051675 Gm. $NaHSO_3$, and 43.55 Cc. will be required to indicate 90 per cent. if 0.25 Gm. of the salt be used for the assay, as directed, for 90 per cent. of 0.25 is 0.225 and $0.225 \div 0.0051675 = 43.54 +$. The Pharmacopœia directs the salt to be added to 50 Cc. of the iodine solution and the mixture set aside in a glass-stoppered bottle for 1 hour with occasional agitation, in order that complete oxidation may be effected. The excess of iodine is then titrated with $\frac{N}{10}$ sodium thiosulphate solution, of which not more than 6.45 Cc. should be required, showing that 43.55 Cc. of the iodine solution have been used by the sodium bisulphite added. This plan has been found more accurate than the gradual addition of iodine solution to a solution of the salt, which invariably gives low results, owing to the escape of sulphur dioxide.

Sodium Borate. $Na_2B_4O_7 + 10H_2O$.—The more familiar name borax is usually applied to this compound, which, although sometimes called sodium biborate, is, as shown by the chemical formula, sodium tetraborate or pyroborate. It is found extensively in different parts of the world, particularly in California, where immense quantities are obtained from the blue mud of certain lakes. Solution and recrystallization are resorted to for the purpose of purification. Considerable quantities of borax are obtained also from crude boric acid, by treating it with sodium carbonate, and from various minerals containing borates of sodium, calcium, and magnesium.

Borax is of special interest in pharmacy on account of its peculiar behavior with other substances. It is incompatible with mucilage of acacia, causing gelatinization, which can, however, be prevented by the presence of sugar; it precipitates many alkaloids from their solution, such as cocaine, morphine, atropine, quinine, etc., except in the presence of glycerin; it forms a damp, almost moist, mixture when triturated with alum; in the presence of glycerin it decomposes alkali bicarbonates with effervescence; and, lastly, while an aqueous solution of borax shows an alkaline reaction toward litmus, a solution in glycerin has a decided acid reaction, which is changed to alkaline upon large dilution with water. This last behavior is also observed with other bodies resembling glycerin, such as mannitol, glucose, etc.

Sodium Bromide. NaBr.—This salt is prepared in a manner similar to potassium bromide, either by decomposing a solution of ferrous bromide with sodium carbonate or by treating a solution of sodium hydroxide with bromine and finally reducing with charcoal any sodium bromate formed.

Sodium bromide is somewhat hygroscopic, but does not deliquesce upon exposure to the air. As in the case of the corresponding potassium salt, some chloride is usually present, which is volumetrically determined with $\frac{N}{10}$ silver nitrate solution, each Cc. of which is equivalent to 0.010224 Gm. NaBr or 0.005806 Gm. NaCl. The rule given under Potassium Bromide (page 489) may be used for finding the exact percentage of sodium chloride contained in any sample. The Pharmacopœia requires the dry salt to contain not less than 97 per cent. of pure NaBr, and demands that not less than 28.5 Cc., and not more than 30 Cc., of $\frac{N}{10}$ $AgNO_3$ solution shall be necessary to precipitate completely 0.3 Gm. of the well-dried salt, potassium chromate being used as an indicator. The lower limit, 28.5, Cc. allowed in the titration will represent 0.2914 Gm. of pure NaBr, which is equal to 97.13 per cent. of the 0.3 Gm. of the salt used, while the higher limit, 30 Cc., allows the presence of not more than 2.96 per cent. sodium chloride, since each 0.223 Cc. of the silver solution used in excess of the theoretical quantity (29.34 Cc.) will represent 1 per cent. of sodium chloride, the difference between 30 and 29.34, or 0.66, divided by 0.223 must indicate 2.96 per cent.

Monohydrated Sodium Carbonate. $Na_2CO_3 + H_2O$.—This is the only form of sodium carbonate now recognized in the Pharmacopœia and is to be decidedly preferred to the former official efflorescent salt containing 10 molecules, or 62.93 per cent., of water of crystallization. It is also to be preferred to the dried sodium carbonate formerly official, as it represents, weight for weight, a larger proportion of sodium carbonate and contains less water. It may be made by crystallizing ordinary sodium carbonate at a temperature above 35° C. (95° F.), and is comparatively stable in the air. When exposed to warm dry air at or above a temperature of 50° C. (122° F.) it effloresces, and at 100° C. (212° F.) loses all of its water, 14.52 per cent. The Pharmacopœia demands not less than 99.5 per cent. of the crystallized monohydrated salt, equivalent to 85 per cent. of anhydrous sodium carbonate. To determine its purity, it is titrated with $\frac{N}{2}$ sulphuric acid, each Cc. of which corresponds to 0.030797 Gm. of the monohydrated or 0.02633 Gm. of the anhydrous salt.

Sodium Chlorate. $NaClO_3$.—This salt may be prepared in a similar manner to potassium chlorate or by decomposing a solution of acid sodium tartrate or sodium silicofluoride with potassium chlorate, ($NaHC_4H_4O_6 + KClO_3 = NaClO_3 + KHC_4H_4O_6$ or $Na_2SiF_6 + 2KClO_3 = 2NaClO_3 + K_2SiF_6$), removing the precipitated potassium compound by filtration, concentrating the solution, and allowing the chlorate to crystallize.

Sodium chlorate is vastly more soluble in both water and alcohol than the corresponding potassium salt; but, like the latter, is readily decomposed when triturated with organic or other easily oxidizable substances, hence it must be handled with care.

Sodium Chloride. NaCl.—There is probably no substance so universally distributed over the world as common salt, nature providing it both in crystalline form, as rock-salt, or in solution, as sea-water and the brine of salt-wells. Rock-salt is extensively mined, but the largest supply of salt is obtained by evaporation of the natural solutions.

Sodium chloride is employed in the manufacture of certain chemicals, but is used rarely in medicine, although an indispensable requisite in the animal system. It is of chief interest to pharmacists as a reagent in the volumetric valuation of silver salts. Commercial sodium chloride sold as table salt is sometimes contaminated with magnesium chloride, which accounts for its hygroscopic character.

The Pharmacopœia requires that official sodium chloride, when dried, shall contain not less than 99 per cent. of pure NaCl, to be determined by titration with $\frac{N}{10}$ $AgNO_3$ solution, using potassium chromate as indicator, each Cc. of which corresponds to 0.005806 Gm. of NaCl; hence 1 Gm. of the dried salt will require not less than 17.05 Cc. for $0.99 \div 0.005806 = 17.05$.

Sodium Citrate. $2Na_3C_6H_5O_7 + 11H_2O$.—This salt is rarely used in medicine, although identical with potassium citrate in therapeutic value, but has received recognition in the Pharmacopœia because it is used in some official preparations. It may be prepared by neutralizing a solution of citric acid with sodium carbonate or bicarbonate, which is then concentrated and allowed to crystallize. To make 100 Gm. of the salt will require 59.09 Gm. of citric acid and 52.37 Gm. of monohydrated sodium carbonate, or 71.3 Gm. of sodium bicarbonate. The salt contains nearly 26.5 per cent. of water of crystallization and effloresces slightly when exposed to dry air. The Pharmacopœia demands 97 per cent. purity, which is determined by converting the salt into carbonate and then titrating with $\frac{N}{2}$ acid, each Cc. of which corresponds to 0.0591 Gm. of the crystallized citrate; hence in the official test 16.4 Cc. of the acid solution will be necessary to indicate 0.9697 Gm. of the salt, which is practically 97 per cent. of the 1 Gm. taken.

The German Pharmacopœia recognizes a freshly prepared effervescent solution of sodium citrate under the name Potio Riveri, River's Draught, which is made by dissolving 4 Gm. of citric acid in 190 Cc. of water and gradually adding to this solution 9 Gm. of crystallized sodium carbonate (equivalent to 3.9 Gm. of the monohydrated salt). The preparation is dispensed before effervescence has entirely ceased, so as to retain considerable of the carbon dioxide in the solution. It closely resembles in character the solution of potassium citrate of the U. S. P., but is considerably weaker.

Sodium Hydroxide. **NaOH**.—The usual method of manufacture of sodium hydroxide, or caustic soda, as it is commonly called, is by decomposition of a solution of sodium carbonate by means of milk of lime, the filtrate, as in the case of caustic potash, being evaporated in silver or iron vessels, and finally allowed to congeal in suitable moulds. The product thus obtained is commercially known as soda by lime. A purer article may be obtained either by purification of commercial caustic soda with alcohol or by direct action of metallic sodium on pure water.

Like potassium hydroxide, sodium hydroxide is very deliquescent, and rapidly absorbs carbon dioxide upon exposure to the air; hence the same care must be observed in its preservation in tightly stoppered green-glass bottles.

The Pharmacopœia makes the same requirements for the absence of other inorganic substances, with the exception of water, as in the case of potassium hydroxide, and demands that official sodium hydroxide shall contain not less than 90 per cent. of absolute NaOH, which is determined volumetrically with normal acid, each Cc. of which is capable of neutralizing 0.03976 Gm. NaOH.

Sodium Hypophosphite. $NaH_2PO_2 + H_2O$.—Like the corresponding potassium salt, this salt may be conveniently made by decomposing a solution of calcium hypophosphite with sodium carbonate or sulphate. After removal of the calcium salt by filtration the solution is evaporated on a water-bath to dryness, with constant stirring for the purpose of granulation.

Sodium hypophosphite is hygroscopic, but more permanent than the potassium salt upon exposure to air, and explodes readily when triturated with nitrates, chlorates, or permanganates, owing to its tendency to oxidation.

The Pharmacopœia requires the official salt to contain not less than 98 per cent. of pure NaH_2PO_2, but, as in the case of potassium hypophosphite, gives no assay process for its determination, as the gravimetric methods alone are reliable; the latter are tedious and hence not well suited for the pharmacist. See explanation under Potassium Hypophosphite.

Sodium Iodide. NaI.—This salt may be prepared by adding iodine to a solution of sodium hydroxide; but since, on the reduction of the resulting sodium iodate with charcoal, some sodium carbonate may be formed, it is preferable to obtain the salt by double decomposition of ferrous or ferroso-ferric iodide with sodium carbonate. The reaction taking place in either case may be explained by the following equations: $FeI_2 + (Na_2CO_3 + 10H_2O) = 2NaI + FeCO_3 + 10H_2O$; $Fe_3I_8 + 4(Na_2CO_3 + 10H_2O) = 8NaI + 4CO_2 + Fe_3(OH)_8 + 36H_2O$. The mixture is boiled so as to facilitate separation of the iron compound by filtration, after which the filtrate is evaporated to dryness, with constant stirring, thus yielding a finely granulated salt.

Sodium iodide crystallizes, in an anhydrous state, at temperatures above 40° C. (104° F.), and this is the salt recognized by the Pharmacopœia; but at ordinary temperatures it takes up nearly 19.5 per cent. of water, and then has the composition $NaI + 2H_2O$; the latter salt is decidedly less hygroscopic than the official anhydrous salt, which readily absorbs moisture from the air. This fact explains the very marked development of heat when strong solutions of the anhydrous salt are made, due to a chemical union of the salt with water, whereas similar solutions of potassium iodide produce a decided reduction of temperature.

Sodium iodide, as well as its aqueous solution, gradually undergoes decomposition upon exposure to light, becoming colored, hence both should be preserved in dark amber-colored bottles.

The official salt must contain not less than 98 per cent. of pure sodium iodide, as indicated by the demand that 0.5 Gm. of the well-dried salt shall require not less than 33 nor more than 34.6 Cc. $\frac{N}{10}$ $AgNO_3$ solution for complete precipitation. Each Cc. of the silver solution corresponds to 0.014878 Gm. of absolute NaI, and hence 0.5 Gm. of the latter would require 33.6 Cc., and any increase above this indicates the presence of sodium bromide or chloride, or both, since these salts have a lower molecular weight than the iodide. The lower limit allowed by the Pharmacopœia, 33 Cc. of the silver solution represents 0.490 (33×0.014878) Gm. of NaI, equal to 98 per cent. Assuming sodium chloride to be the only foreign haloid salt present, the higher limit, 34.6 Cc., indicates an excess of 1 ($34.6 - 33.6$) Cc. over the theoretical quantity, which corresponds to 1.98 per cent. of sodium chloride, as each 0.5252 Cc. represents 1 per cent.

Sodium Nitrate. $NaNO_3$.—The immense nitre-beds of Chili and Peru furnish this salt in a more or less crude state; it is commercially known as Chili saltpetre, or cubic nitre, and is purified by repeated solution and crystallization.

Sodium nitrate is of comparatively little interest in pharmacy, but is extensively employed in the manufacture of nitric and sulphuric acids, potassium nitrate, etc. It differs from ordinary saltpetre in being hygroscopic and in its greater solubility in water and alcohol.

Sodium Nitrite. $NaNO_2$.—This salt is interesting chiefly as the source of nitrous acid in the official process for the manufacture of ethyl nitrite in the preparation of spirit of nitrous ether. When sodium nitrate is heated with charcoal, starch, or similar reducing agents, sodium nitrite is formed; but a better process consists in heating fused sodium nitrate for some time with lead in thin sheets, whereby the lead is gradually converted into lead oxide or litharge and the sodium salt is reduced to nitrite; thus, $2NaNO_3 + Pb_2 = 2NaNO_2 + 2PbO$. The fused mass is lixiviated with water, the solution treated with carbon dioxide to remove any lead possibly held in solution, filtered, and finally allowed to crystallize. By repeated recrystallization a very pure salt can be obtained containing 98 per cent. and over of absolute sodium nitrite.

On account of its deliquescent character and ready oxidation to nitrate upon exposure to air, the salt must be carefully preserved in tightly closed bottles.

The value of sodium nitrite depends upon the proportion of $NaNO_2$ present, which should not be less than 90 per cent., and is determined volumetrically by titration with $\frac{N}{10}$ potassium permanganate solution. From the equation $2KMnO_4 + 5NaNO_2 + 3H_2SO_4 = 5NaNO_3 + K_2SO_4 + 2MnSO_4 + 3H_2O$ it appears that 313.96 Gm. of potassium permanganate are capable of oxidizing 342.85 Gm. of sodium nitrite, and hence 1 Cc. of $\frac{N}{10}$ $KMnO_4$ solution, containing 0.0031396 Gm. of the salt, corresponds to 0.0034285 Gm. of pure $NaNO_2$. To indicate 90 per cent. of 1 Gm. in the official test will require 26.25 ($0.90 \div 0.0034285$) Cc. of the potassium permanganate solution, which is the quantity actually consumed, for $30 - 3.75 = 26.25$.

pyrophosphoric acid by the further elimination of water. Two molecules of the crystallized phosphate yield one molecule of the pyrophosphate; thus, $2(Na_2HPO_4 + 12H_2O) = Na_4P_2O_7 + 25H_2O$. The dry residue is dissolved in water, and the solution set aside to crystallize.

The crystals of sodium pyrophosphate are difficult to reduce to fine powder, and are far less soluble in water than those of the orthophosphate.

Sodium Salicylate. $NaC_7H_5O_3$ or $C_6H_4(OH)COONa$.—The official salt may be conveniently obtained by mixing sodium bicarbonate 10 parts and salicylic acid 16.5 parts with distilled water 10 parts, in a glass or porcelain vessel, and, when effervescence has ceased, evaporating the solution, at a temperature not exceeding 60° C. (140° F.), to dryness. It is essential that the solution be slightly acid; hence, if necessary, a trifling addition of salicylic acid may be made, since alkali salicylates, in the presence of an excess of alkali, absorb oxygen from the air and become colored. Sodium bicarbonate and pure monocarbonate are better suited than sodium hydroxide for neutralizing the acid, since strong bases are likely to form different salts with salicylic acid, such as $Na_2C_7H_4O_3$, although the acid is monobasic; these so-called secondary salicylates are less permanent and less soluble in water than the normal salts.

All contact with iron must be carefully avoided in the preparation of this salt, owing to the delicate reaction of salicylic acid with that metal, and filtration through ordinary filter-paper will frequently color a solution of the salicylate; hence cotton or glass-wool is preferable for straining.

The Pharmacopœia demands almost absolute purity for this salt, 99.5 per cent., which may be determined by converting it into carbonate by ignition, and then titrating with $\frac{N}{2}$ acid, each Cc. of which corresponds to 0.079445 Gm. of the original salt; hence in the official test 12.52 Cc. of the acid solution will be necessary to indicate 0.995 Gm. of sodium salicylate (99.5 per cent. of 1 Gm.) as $0.995 \div 0.079445 = 12.52$.

Sodium Sulphate. $Na_2SO_4 + 10H_2O$.—This salt is daily obtained as a by-product in numerous chemical processes, such as the manufacture of hydrochloric and nitric acids and magnesium carbonate, as well as the generation of carbon dioxide from sodium bicarbonate with sulphuric acid, in the manufacture of carbonated waters. It is purified, if necessary, by recrystallization.

The official salt, commonly known as Glauber's Salt, contains 55.9 per cent. of water of crystallization and effloresces rapidly upon exposure to air.

For convenience in dispensing, the German Pharmacopœia directs the preparation of dried sodium sulphate, by exposing the crystallized salt to a moderate heat until its weight has been reduced to one-half, as in the case of dried sodium carbonate. The dehydrated salt is in the form of a white powder and represents double the weight of the crystallized salt.

Effervescent sodium sulphate is directed by the British Pharmacopœia to be made from the anhydrous salt in the same manner as stated under sodium phosphate. It contains about 25 per cent. Na_2SO_4.

Sodium Sulphite. $Na_2SO_3 + 7H_2O$.—Normal sodium sulphite is obtained by first preparing a solution of the acid sulphite, as explained under sodium bisulphite, and then adding a weight of sodium carbonate equal to that first used, when a neutral salt will be formed; thus, $2NaHSO_3 + Na_2CO_3 = 2Na_2SO_3 + CO_2 + H_2O$. The solution is then evaporated and allowed to crystallize.

The official salt contains 50 per cent. of water of crystallization, and is liable to be contaminated with the same impurities as the bisulphite; it effloresces upon exposure to air and, like the latter salt, is gradually converted into sulphate. The Pharmacopœia requires that the salt shall contain at least 96 per cent. of crystallized Na_2SO_3, which is determined by means of iodine solution, whereby all sulphite present is converted into sulphate. According to the equation, $Na_2SO_3.7H_2O + I_2 = Na_2SO_4 + 2HI + 6H_2O$, each Cc. $\frac{N}{10}$ iodine solution, containing 0.01259 Gm. of iodine, is capable of oxidizing 0.01252 Gm. of the crystallized sulphite; hence 38.34 Cc. will be required for 0.5 Gm. of the official salt, as 96 per cent. of 0.5 is 0.48 and $0.48 \div 0.01252 = 38.33 +$. The official test is made, as in the case of the bisulphite, by adding an excess of the iodine solution, and after complete oxidation has been effected titrating the excess with sodium thiosulphate solution.

Sodium Thiosulphate. $Na_2S_2O_3 + 5H_2O$.—This salt, wrongly called sodium hyposulphite, may be obtained in various ways, such as boiling a solution of sodium sulphite with sulphur ($Na_2SO_3 + S = Na_2S_2O_3$), adding iodine to a solution of sodium sulphite and sulphide ($Na_2SO_3 + Na_2S + I = Na_2S_2O_3 + 2NaI$), boiling sulphur with solution of soda ($6NaOH + S_{12} = Na_2S_2O_3 + 2Na_2S_5 + 3H_2O$), etc.; the process employed on a large scale, however, consists in decomposition of calcium thiosulphate in solution by means of sodium carbonate or sulphate, insoluble calcium carbonate or sulphate being precipitated, while sodium thiosulphate remains in solution and is recovered, after filtration, by crystallization; the reaction may thus be indicated, $CaS_2O_3 + Na_2CO_3 = Na_2S_2O_3 + CaCO_3$. Calcium thiosulphate is obtained either from the residue left in the manufacture of sodium carbonate by the Leblanc process, known as alkali-waste, or from the gas-lime left in the purification of illuminating gas by dry lime. Both of these residues contain calcium sulphides which, upon exposure to the air, undergo oxidation and are converted into thiosulphate.

chlorine. If 7 Gm. of solution of chlorinated soda be taken, as directed in the official test, 48 Cc. of $\frac{N}{10}$ sodium thiosulphate solution will be required to discharge the color caused by the liberated iodine, in order to indicate 2.4 per cent. of chlorine, for 2.4 per cent. of 7 is 0.168, and $0.168 \div 0.003518 = 47.75 +$.

A preparation very similar to the foregoing is the solution of chlorinated potassa known as Javelle water, or eau de Javelle; it is prepared by substituting an equivalent quantity of potassium carbonate for the sodium carbonate in the above process.

Solution of Sodium Arsenate.—Like Fowler's Solution, this preparation may be more conveniently considered with the official compounds of arsenic.

Besides the official salts of sodium, the following are of interest to pharmacists:

Effervescent Sodium Citro-tartrate.—This name is applied in the British Pharmacopœia to a granular combination of sodium bicarbonate 510 Gm., tartaric acid 270 Gm., citric acid 180 Gm., and sugar 150 Gm. The ingredients, in fine powder, are thoroughly mixed and the mixture granulated by placing it in a dish heated to between 93° and 104° C. (197.4° and 219.2° F.) and stirring properly as the powder begins to soften and agglutinate. The resulting granular mixture when dissolved in water produces both citrate and tartrate of sodium, with the elimination of carbon dioxide.

Sodium Ethylate. C_2H_5ONa.—This salt, also known as caustic alcohol, is obtained by direct action of metallic sodium on absolute alcohol, the metal being added in small pieces at a time as long as the evolution of hydrogen continues, and the mixture kept cool by immersing the flask in cold water. The salt may be preserved in the form of crystals or powder in well-stoppered bottles. The British Pharmacopœia directs a solution of sodium ethylate to be made by dissolving 22 grains of metallic sodium in 1 fluidounce of absolute alcohol; it is a colorless, syrupy liquid, containing 18 per cent. of the salt, and becoming brown by keeping.

Sodium Glycerophosphate. $C_3H_5(OH)_2Na_2PO_4 + H_2O$.—This compound is met with both in the form of a very hygroscopic salt of alkaline reaction, and as a 50 per cent. aqueous solution. It is usually obtained by mutual decomposition between a solution of barium or calcium glycerophosphate and one of sodium carbonate or sulphate, but may also be made by dissolving sodium carbonate in an aqueous solution of glycerophosphoric acid and concentrating the resulting solution in a vacuum apparatus.

Sodium Sulphovinate or Ethylsulphate. $NaC_2H_5SO_4 + H_2O$.—When sulphuric acid is added gradually to an equal weight of alcohol, sulphovinic or ethylsulphuric acid is formed; thus, $C_2H_5OH + H_2SO_4 = C_2H_5HSO_4 + H_2O$; this can be neutralized by adding barium carbonate in excess, filtering the mixture, and decomposing the solution of barium sulphovinate by a solution of sodium carbonate or sulphate. After filtration the clear liquid is evaporated at a moderate heat and crystallized. The salt is very soluble in water and also in alcohol and glycerin.

Sodium Tartrate. **$Na_2C_4H_4O_6 + 2H_2O$ or $(CHOH)_2(COONa)_2.2H_2O$.**—This salt may be prepared, like the citrate, by simple substitution of tartaric acid for citric acid. To make 100 parts requires 65.19 parts of tartaric acid and 125.73 parts of crystallized sodium carbonate, or 74.09 parts of bicarbonate.

Sodium Valerianate. **$NaC_5H_9O_2$ or $(CH_3)_2CHCH_2COONa$.**—This salt may be made by neutralizing valerianic acid with caustic soda or sodium carbonate; the solution is evaporated to dryness and the heat then continued until the salt fuses. If the valerianic acid is contaminated with amyl valerianate (apple oil), this will separate, and, floating as an oily liquor on the solution, can be removed.

CHAPTER XLIII.

THE COMPOUNDS OF LITHIUM.

FIVE lithium salts are recognized in the Pharmacopœia together with one effervescent preparation of a salt. A peculiarity of all lithium salts, by which they can readily be distinguished from other alkali salts, is their complete solubility in a mixture of equal volumes of alcohol and ether, after conversion into the chloride.

The following is a list of the official lithium preparations:

Official English Name.	Official Latin Name.
Lithium Benzoate,	Lithii Benzoas.
Lithium Bromide,	Lithii Bromidum.
Lithium Carbonate,	Lithii Carbonas.
Lithium Citrate,	Lithii Citras.
Effervescent Lithium Citrate,	Lithii Citras Effervescens.
Lithium Salicylate,	Lithii Salicylas.

Lithium Benzoate. $LiC_7H_5O_2$ or C_6H_5COOLi.—This salt is most conveniently prepared from the carbonate, by suspending the same in hot water and adding benzoic acid as long as effervescence continues; the filtrate is evaporated on a water-bath to dryness, with constant stirring, or may be concentrated and set aside to crystallize. To make 100 parts of the salt will require 29 parts of lithium carbonate and 95.3 parts of benzoic acid, the reaction being as follows: $2HC_7H_5O_2 + Li_2CO_3 = 2LiC_7H_5O_2 + CO_2 + H_2O$.

The salt is permanent in the air and very soluble in water, but less so in alcohol. The Pharmacopœia requires 98.5 per cent. purity, which is determined gravimetrically by converting the salt into sulphate, and weighing as such, after ignition. Each Gm. of lithium benzoate will yield 0.43 Gm. of sulphate, and in the official test 0.5 Gm. is required to yield not less than 0.210 nor more than 0.216 Gm., the ammonium benzoate formed being volatilized, whereas the lithium sulphate remains after ignition as a non-volatile residue. The theoretical yield, if the salt be 98.5 per cent. pure, in the official test would be 0.212 + Gm.

Lithium Bromide. LiBr.—For the preparation of this salt diluted hydrobromic acid may be neutralized with lithium carbonate, or the latter salt may be agitated in a flask with a hot solution of ferrous bromide. The first method is probably the most desirable. Owing to the very deliquescent character of the salt it is not readily crystallized, and is preferably obtained in granular powder form by evaporating the solution to dryness on a water-bath.

Lithium bromide contains about 92 per cent. of bromine, a larger proportion than any other salt. It is very soluble in water and alcohol, and also soluble in ether, and must be carefully preserved in well-stoppered bottles.

The salt is likely to be contaminated with lithium chloride (due to chlorine in the bromine), and the Pharmacopœia requires not less than 97 per cent. of pure lithium bromide. The official test for the limit (1.75 per cent.) of other alkalies depends upon the solubility of lithium chloride in the amyl alcohol, in which other alkali chlorides are insoluble. The degree of purity is determined volumetrically by means of $\frac{N}{10}$ $AgNO_3$ solution; 0.20 Gm. of the dried salt must require not less than 22.5 Cc. nor more than 23.9 Cc. of the silver solution for complete precipitation, potassium chromate being used as indicator. Each Cc. of the silver solution corresponding to 0.008634 Gm. of lithium bromide, 0.2 Gm. of absolutely pure LiBr, would require 23.16 + Cc. The presence of other alkali bromides would cause a lesser quantity of the silver solution to suffice. The higher pharmacopœial limit, 23.9 Cc., is intended to limit the amount of lithium chloride present, and as some chloride is presumably present in all lithium bromide its presence will counteract the effect of other alkali bromides, and thus the titration may show a pure salt when in reality both impurities are present.

Lithium Carbonate. Li_2CO_3.—The carbonate, the parent salt of the other lithium compounds, is obtained from the mineral lepidolite, a mixture of silicates and fluorides of potassium, sodium, aluminum, and lithium. By digestion with sulphuric acid impure lithium sulphate is obtained, which is freed from the other salts by crystallization, treatment with milk of lime, etc. The final solution of alkali hydroxides is mixed with ammonium carbonate, whereby the lithium carbonate is precipitated; or the mixed alkali hydroxides may be converted into chlorides, and the solution then treated with ammonium carbonate. For the purpose of purification lithium carbonate may be suspended in water and treated with carbon dioxide, when an acid carbonate, $LiHCO_3$, will be formed and enter into solution, upon heating which pure lithium carbonate will be precipitated.

Lithium carbonate is the least soluble of all alkali carbonates, and is, moreover, only a little more than half as soluble in boiling water as in cold water. It occurs in commerce as a light, odorless powder.

The Pharmacopœia demands that if 0.5 Gm. of the salt be dissolved in 20 Cc. of normal acid, not more than 6.6 Cc. of normal alkali shall be required to neutralize the excess of acid, indicating at least 98.5 per cent. of pure Li_2CO_3. As each Cc. of normal acid corresponds to 0.036755 Gm. of the pure salt, 0.4925 (98.5 per cent. of 0.5) Gm. will require 13.4 Cc. of the acid, for $0.4925 \div 0.036755 = 13.4$.

Lithium Citrate. **$Li_3C_6H_5O_7 + 4H_2O$ or $C_3H_4OH(COOLi)_3 + 4H_2O$.**—This salt can be prepared by adding lithium carbonate to a solution of citric acid until the latter is neutralized, then concentrating the solution and allowing it to crystallize. As shown by the equation $2(H_3C_6H_5O_7 + H_2O) + 3Li_2CO_3 + 3H_2O = 2(Li_3C_6H_5O_7 + 4H_2O) + 3CO_2$, 2 molecules or 417 Gm. of citric acid require 3 molecules or 220.53 Gm. of lithium carbonate, the yield of crystallized lithium citrate being about 560 Gm. If the solution be evaporated to dryness and the residue heated to 140° C. (284° F.) an anhydrous salt will be obtained identical with that formerly recognized in the U. S. P.

The Pharmacopœia requires 98.5 per cent. purity for lithium citrate, which is determined gravimetrically, as in the case of the benzoate, except that ammonium sulphate is not used, the citrate being ignited and treated with a little nitric and sulphuric acids to convert it into sulphate. The equations $2(Li_3C_6H_5O_7 + 4H_2O) + O_{18} = 3Li_2CO_3 + 9CO_2 + 13H_2O$ and $3Li_2CO_3 + 3H_2SO_4 = 3Li_2SO_4 + 3CO_2 + 3H_2O$ show that 2 molecules or 560.16 Gm. of crystallized lithium citrate will yield 3 molecules or 327.93 Gm. of lithium sulphate, and hence 1 Gm. of the former will yield 0.5854 Gm. of the latter. In the official test 0.5 Gm. of the anhydrous salt is required to yield not less than 0.387 nor more than 0.394 Gm. of sulphate. Lithium citrate contains about 25.5 per cent. of water of crystallization, and as the salt is deliquescent in moist air, the Pharmacopœia directs that the assay shall be made with anhydrous salt; if absolutely pure, the 0.5 Gm. of citrate will yield 0.3933 + Gm. of sulphate; and if 98.5 per cent. pure, the yield will be 0.3875 + Gm. Any yield of sulphate residue greater than the highest theoretical will therefore indicate the presence of other alkalies or impurities.

Both the anhydrous salt in powder-form and the crystallized salt occur in commerce.

Investigation has shown that the commercial lithium citrate offered in this country is by no means uniform in composition, varying from an anhydrous salt to one containing one or more molecules of water; moreover, according to L. F. Kebler, the anhydrous salt is more or less deliquescent, but becomes non-deliquescent after a certain amount of moisture has been absorbed.

Effervescent Lithium Citrate.—This preparation contains about 5 per cent. of crystallized lithium citrate, and is made by the general process directed in the Pharmacopœia for the manufacture of all granular effervescent salts. It has already been considered in the Chapter on Granular Effervescent Salts (see page 410).

Lithium Salicylate. **$LiC_7H_5O_3$ or $C_6H_4(OH)COOLi$.**—This salt may be prepared by heating a mixture of 44 parts of salicylic acid, 12 parts of lithium carbonate, and 100 parts of water until effervescence ceases; it is then filtered and the solution evaporated to dryness. As in the case of sodium salicylate, a slight excess of acid is necessary to avoid discoloration of the finished product, and contact with metal must be carefully avoided.

The Pharmacopœia requires for lithium salicylate 98.5 per cent. purity, to be determined gravimetrically exactly as in the case of lithium benzoate. Each Gm. of lithium salicylate, if absolutely pure, will yield 0.382 Gm. of sulphate. In the official test 0.5 Gm. of the salt is required to yield not less than 0.188 nor more than 0.192 Gm. of sulphate; the theoretical yield, if the salt be 98.5 per cent. pure, would be 0.188 + Gm.

CHAPTER XLIV.

THE COMPOUNDS OF AMMONIUM.

ALTHOUGH, thus far, all efforts to isolate the basylous radical of ammonium salts have failed, the existence of the hypothetical body NH_4 must be assumed, as, without it, it would be impossible to explain the formation and composition of a large and important class of compounds in accordance with accepted modern views regarding the replacement of hydrogen in acids. The decomposition of sodium amalgam by means of ammonium chloride, resulting in the production of sodium chloride and a new spongy amalgam having a metallic lustre, points strongly to the metallic character of the radical called ammonium. The indirect source of all ammonium salts is the gaseous body ammonia, NH_3, which may be looked upon as ammonium hydroxide minus water, $NH_4OH - H_2O = NH_3$; a characteristic feature of these salts is their complete volatilization upon application of heat.

The Pharmacopœia recognizes 7 salts of ammonium, 4 preparations of the salts, and 3 solutions of the hydroxide, as follows:

Official English Name.	Official Latin Name.
Ammonium Benzoate,	Ammonii Benzoas.
Ammonium Bromide,	Ammonii Bromidum.
Ammonium Carbonate,	Ammonii Carbonas.
Ammonium Chloride,	Ammonii Chloridum.
Ammonium Iodide,	Ammonii Iodidum.
Ammonium Salicylate,	Ammonii Salicylas.
Ammonium Valerate,	Ammonii Valeras.
Ammonia Water,	Aqua Ammoniæ.
Stronger Ammonia Water,	Aqua Ammoniæ Fortior.
Liniment of Ammonia,	Linimentum Ammoniæ.
Solution of Ammonium Acetate,	Liquor Ammonii Acetatis.
Spirit of Ammonia,	Spiritus Ammoniæ.
Aromatic Spirit of Ammonia,	Spiritus Ammoniæ Aromaticus.
Troches of Ammonium Chloride,	Trochisci Ammonii Chloridi.

Ammonium Benzoate. $NH_4C_7H_5O_2$ or $C_6H_5COONH_4$.—When benzoic acid is added to diluted ammonia water, the acid is neutralized and ammonium benzoate is formed, which, remaining in solution, may be obtained in colorless crystals, if the liquid be concentrated by aid of a moderate heat and set aside. As ammonium salts are readily decomposed by heat, the liquid should be kept alkaline by the occasional addition of ammonia water during evaporation. To prepare 100 Gm. of the salt requires 87.75 Gm. of benzoic acid and 123 Gm. of the official ammonia water.

The Pharmacopœia requires that ammonium benzoate shall contain not less than 98 per cent. of pure $NH_4C_7H_5O_2$, but gives no directions for determining the purity, although tests are given for proving the absence of chlorides and sulphates and also heavy metals.

Ammonium Bromide. NH_4Br.—Decidedly the best method of preparing this salt is by double decomposition between boiling hot concentrated solutions of ammonium sulphate and potassium bromide, when, upon cooling, the newly formed potassium sulphate is precipitated, while ammonium bromide remains in solution. To facilitate removal of the potassium sulphate, alcohol is usually added to the cooled liquid. The salt may be obtained in granular form by decanting the solution, concentrating it, and evaporating to dryness with constant stirring.

Ammonium bromide may also be obtained quite pure by heating in a retort, on a sand-bath, an intimate mixture of potassium bromide and dried ammonium sulphate, and subliming the vapors of ammonium bromide in a suitable condenser.

The Pharmacopœia demands that ammonium bromide shall contain not less than 97 per cent of pure NH_4Br, which may be determined volumetrically with $\frac{N}{10}$ $AgNO_3$ solution, each Cc. of which corresponds to 0.009729 Gm. of the pure salt. In the official test 0.3 Gm. taken should therefore require not more than 31.6 Cc. of the silver solution, indicating the absence of more than 3 per cent. of ammonium chloride, the rule given under Potassium Bromide being also applicable in this case, and each 0.2565 Cc. of the silver solution used in excess of the theoretical requirement for pure NHBr, 30.83 + Cc. indicating 1 per cent. of ammonium chloride.

Ammonium Carbonate. $NH_4HCO_3NH_4NH_2CO_2$.—As shown by the chemical formula, the official salt is not the normal carbonate, which would have the composition $(NH_4)_2CO_3$, but is a mixture of acid ammonium carbonate and ammonium carbamate. It is obtained on an extensive scale by heating ammonium chloride with an excess of chalk and condensing the resulting vapors in leaden chambers; it is afterward resublimed. The decomposition is accompanied by the splitting off of ammonia and water; hence the composition of the sublimate, as given in the Pharmacopœia: $4NH_4Cl + 2CaCO_3 = NH_4HCO_3NH_4NH_2CO_2 + 2CaCl_2 + NH_3 + H_2O$.

The commercial ammonium carbonate is usually accompanied by empyreuma, to which its peculiar tarry odor is due, and for pharmaceutical purposes only the purified article should be employed. Owing to the rapid deterioration of the salt on exposure to air, from loss of both ammonia and carbon dioxide, it should be preserved in tightly closed bottles, the best container being a wide-mouth fruit jar provided with a rubber ring and metal clasp for hermetically sealing the glass top. Only firm translucent pieces of ammonium carbonate should be used, as the opaque friable condition is indicative of chemical change causing conversion of the salt into acid carbonate or bicarbonate.

When the official ammonium carbonate is dissolved in water it is converted into the so-called sesquicarbonate, a mixture of acid and normal carbonate; thus, $NH_4HCO_3NH_4NH_2CO_2 + H_2O = NH_4HCO_3(NH_4)_2CO_3$. The Pharmacopœia requires that the official salt shall contain not less than 97 per cent. of the official compound and yield not less than 31.58 per cent. of ammonia gas. To determine the purity, 2 Gm. of the salt are dissolved in a mixture of 50 Cc. each of water and normal acid, the solution boiled to expel all carbon dioxide and the excess of acid then titrated by means of normal KOH solution. Not less than 37.3 (50 − 12.7) Cc. of normal acid should be required to indicate 97 per cent. purity, as each Cc. corresponds to 0.052003 Gm. of $NH_4HCO_3.NH_4NH_2CO_2$, and 1.94 (97 per cent. of 2) Gm. ÷ 0.052003 = 37.3 +.

Ammonium Chloride. **NH_4Cl.**—Crude ammonium chloride is obtained by neutralizing the ammoniacal gas-liquors, condensed in the preparation and purification of illuminating-gas from coal, with hydrochloric acid, evaporating the solution to dryness and subliming the salt in iron vessels. This product, being usually contaminated with iron, is, for pharmaceutical purposes, purified by adding ammonia water to a hot solution of the salt, filtering to remove the precipitated ferric hydroxide, and evaporating the filtrate with constant stirring, so as to form a granular powder.

The Pharmacopœia requires not less than 99.5 per cent. purity, which is determined by titrating a solution of 0.1 Gm. of the salt with $\frac{N}{10}$ $AgNO_3$ solution, each Cc. of which corresponds to 0.005311 Gm. of pure NH_4Cl, and 0.0995 (99.5 per cent. of 0.1 Gm.) ÷ 0.005311 = 18.74; hence at least 18.7 Cc. of the silver solution will be required for complete precipitation, potassium chromate being used as an indicator.

Ammonium Iodide. **NH_4I.**—This salt is most conveniently prepared by double decomposition between potassium iodide and ammonium sulphate dissolved in a small quantity of boiling water; when the mixture has cooled, alcohol is added to insure a more perfect separation of the newly formed potassium sulphate, and the solution of ammonium iodide is filtered and evaporated to dryness, constantly stirring. The reaction is as follows: $2KI + (NH_4)_2SO_4 = 2NH_4I + K_2SO_4$

Ammonium iodide must be preserved in tightly stoppered dark bottles, as it is very hygroscopic and is readily decomposed when exposed to air and light. As the Pharmacopœia directs, the salt should never be dispensed after it has become deeply colored, but may be restored to its original condition by dissolving in as little water as possible, adding solution of ammonium sulphide until the color is discharged, then filtering to remove the precipitated sulphur, and evaporating on a water-bath to dryness. The ammonium sulphide added undergoes decomposition, uniting with the free iodine to form ammonium iodide, while sulphur is precipitated at the same time; thus, $(NH_4)_2S + I_2 = 2NH_4I + S$.

The official test for the presence of ammonium bromide and chloride depends upon the very sparing solubility of silver iodide in ammonia water; hence any turbidity or precipitate produced in the ammoniacal filtrate upon the addition of nitric acid must be due to the presence of silver bromide or chloride. If the 0.25 Gm. of ammonium iodide directed to be used in the official test consist of pure NH_4I, 17.38 + Cc. of the silver solution will be required for complete precipitation, as each Cc. corresponds to 0.014383 Gm. of pure NH_4I and $0.25 \div 0.014383 = 17.38$; the presence of ammonium bromide or chloride would increase this quantity, owing to the lower molecular weights of the latter compounds. As only 97 per cent. of purity is required, the 16.9 Cc. of silver solution ordered will suffice to precipitate all the ammonium iodide corresponding to such purity, for 97 per cent. of 0.25 is 0.2425 and $0.2425 \div 0.014383 = 16.86 +$. As no silver bromide or chloride will be formed until all ammonium iodide has been decomposed, less than 0.2425 Gm. or 97 per cent. of the latter salt taken will allow of their formation and consequent solution in the ammoniacal liquid; hence the appearance of cloudiness within ten minutes after acidulating with nitric acid will indicate that more than 3 per cent. of ammonium bromide or chloride was contained in the sample.

Ammonium Salicylate. $NH_4C_7H_5O_3$ or $C_6H_4(OH)COONH_4$.—This salt is conveniently prepared by neutralizing ammonia water by means of salicylic acid and evaporating the solution to dryness. To make 100 parts of ammonium salicylate will require 89 parts of salicylic acid and 109.98 parts of 10 per cent. ammonia water.

Ammonium Valerate. $NH_4C_5H_9O_2$ or $(CH_3)_2CHCH_2COONH_4$.—This salt, also known as ammonium valerianate, is prepared by neutralizing pure valeric acid with ammonia, conducting the gas directly into the acid, so as to avoid the presence of water, which insures more perfect crystals.

When perfectly neutral, ammonium valerate has little disagreeable odor, but as the salt is prone to decomposition, it is frequently accompanied by the characteristic odor of valeric acid. The acid reaction sometimes observed in an aqueous solution of the salt is due to decomposition, which is indicated also by the pronounced odor of the free acid floating on the surface of the solution: valeric acid being monobasic, there can be no acid salt of the same; hence any free acid present is due to loss of ammonia in the normal salt.

The salt is rarely prescribed except in the form of the elixir of ammonium valerate; in the preparation of this elixir it is customary to dissolve the salt in aromatic elixir, neutralizing any free acid present by means of ammonium carbonate.

Ammonium valerate must be carefully preserved in tightly stoppered vials.

Ammonia Water.—Under this name the Pharmacopœia recognizes an aqueous solution of ammonia containing 10 per cent. by weight of the gas. It is prepared, on a large scale, by liberating ammonia from ammonium chloride or sulphate, by the aid of lime and heat, and conducting the gas into a series of receivers containing cold water, where it is rapidly absorbed; the residue in the retort consists of either calcium chloride or sulphate, as the case may be; thus, $2NH_4Cl$ or $(NH_4)_2SO_4 + Ca(OH)_2 = 2NH_3 + (CaCl_2$ or $CaSO_4) + 2H_2O$. Ammonia water is also made by mixing the ammoniacal liquors of gas-works with milk of lime, heating, and conducting the gas into water; when made by this process the solution generally is less pure, being accompanied by empyreuma.

Ammonia gas is very soluble in water, which at 0° C. (32° F.) is capable of taking up 1050 volumes of the gas, and even at 15° C. (59° F.) retains 727 volumes in solution. The official ammonia water contains about 125 volumes of gas—that is, 1 Cc. holds 125 Cc. of ammonia gas in solution.

Different grades of strength of ammonia water are found in commerce, of which that designated as 16° corresponds to the official 10 per cent. solution; but it must be borne in mind that ammonia water is prone to deteriorate, by loss of ammonia gas, when kept in loosely stoppered vessels, such as carboys, especially if stored in a warm place. Ammonia water should be preserved in glass-stoppered bottles, although sound corks may be used if not allowed to come in contact with the liquid, by covering with prepared bladder, as small particles of cork allowed to fall into the liquid soon impart a yellowish color to the same.

Ammonia water is frequently called *spirit of hartshorn* by the public; in the British Pharmacopœia it is recognized as *solution of ammonia*, and in the German Pharmacopœia as *solution of caustic ammonia*.

The strength of ammonia water is determined by titration with normal acid, each Cc. of which requires 0.01693 Gm. NH_3 for neutralization. The Pharmacopœia directs that 3 Cc. of ammonia water be accurately weighed, diluted with 50 Cc. of water, and then titrated with normal acid; the number of Cc. of the acid used is multiplied by 1.693 (0.01693×100) and divided by the weight taken of the sample, when the quotient will express the percentage of ammonia gas present.

Stronger Ammonia Water.—This preparation differs from the preceding only in strength, containing 28 per cent. by weight of ammonia gas, and is prepared in a similar manner, except that the gas must be conducted into the cold water for a longer period of time, so that a greater amount may be absorbed.

Stronger ammonia water is not used in medicine, but has been found a very convenient source of supply for small quantities of pure ammonia gas, by simply heating in a flask provided with a delivery-tube, and for this purpose has been officially recognized. It can also be employed for the manufacture of weaker solutions of ammonia, which can be prepared of any desired strength by diluting the stronger ammonia water with plain water in proper proportions by weight, as explained on page 73. On account of the readiness with which all solutions of ammonia part with the gas upon elevation of temperature, care should be exercised in opening bottles containing stronger water of ammonia, as serious accidents have been known to occur from the sudden expulsion of liquid upon loosening the stopper, due to accumulation of gas in the vessel.

The commercial grade known as 26° ammonia water corresponds to the official stronger solution. It should be purchased only in glass-stoppered bottles and preserved in a cool place. The official strong solution of the British Pharmacopœia, liquor ammoniæ fortis, contains 32.5 per cent. of ammonia gas (by weight).

The strength of the preparation is determined volumetrically, like that of the weaker solution, with normal acid.

Spirit of Ammonia.—This is an alcoholic solution of ammonia, identical in strength with the official ammonia water, namely, 10 per cent. by weight of gas. It is prepared by heating stronger ammonia water in a flask, at a temperature not exceeding 60° C. (140° F.), to avoid the transfer of aqueous vapor as far as possible, and conducting the gas into recently distilled alcohol. The object of the pharmacopœial direction to use recently distilled alcohol kept in glass vessels is to avoid contamination with organic matters, always present more or less in alcohol as ordinarily preserved, and likely to cause coloration of the liquid upon addition of ammonia.

Spirit of ammonia is intended to be used in place of water of ammonia whenever addition of the latter would cause turbidity in resinous alcoholic solutions.

Aromatic Spirit of Ammonia.—A hydro-alcoholic solution of normal ammonium carbonate, pleasantly flavored with essential oils. It contains 70 per cent. by volume of alcohol, 1 per cent. of oil of lemon, and 0.1 per cent. each of oils of lavender and nutmeg. When official ammonium carbonate is treated with alcohol a portion of the salt enters into solution, the carbamate being converted into carbonate, while the acid carbonate remains undissolved; therefore the Pharmacopœia directs in the formula for this preparation that ammonia water shall be added to the ammonium carbonate before the admixture of the alcoholic solution of essential oils. This causes a change of the official salt into normal carbonate, which is perfectly soluble in alcohol; the change effected may be readily explained as follows: $NH_4HCO_3NH_4NH_2CO_2 + NH_3 + H_2O = 2(NH_4)_2CO_3$. In order to insure the complete conversion of the ammonium salt, it has been found advantageous to allow the mixture of ammonium carbonate solution and ammonia water to stand for twelve or twenty-four hours and then to add to it the alcoholic solution of oils, otherwise a saline precipitate may form.

Since 156.01 parts of official ammonium carbonate will yield 190.82 parts of the normal carbonate, the finished solution, if properly made, will contain 41.58 + Gm. of the latter salt in a liter, or each Cc. will contain 0.0415 + Gm.

Solution of Ammonium Acetate.—This preparation, also known as Spirit of Mindererus, is an aqueous solution of ammonium acetate, containing also small amounts of acetic and carbonic acids. It is preferably prepared fresh when wanted, as when kept on hand for some time it gradually loses carbon dioxide and absorbs ammonia from the air, finally acquiring an alkaline taste. Prepared according to the official formula, by dissolving 5 Gm. of ammonium carbonate (in firm pieces) in 100 Cc. of diluted acetic acid, the finished product will contain 0.071 + Gm. of ammonium acetate in each Cc. (about 33 grains in each fluidounce), together with a trifling amount of acetic acid; to the latter, as well as to the carbon dioxide remaining in solution, the pleasant, refreshing taste of the preparation is due. 100 Cc. of diluted acetic acid contain 6.054 Gm. of absolute acetic acid, of which, according to the equation $NH_4HCO_3NH_4NH_2CO_2 + 3HC_2H_3O_2 = 3NH_4C_2H_3O_2 + H_2O + 2CO_2$, 5.728 + Gm. are required to saturate 5 Gm. of ammonium carbonate.

The following unofficial salts of ammonium are sometimes used:

Ammonium Bicarbonate. **NH_4HCO_3.** This salt has been mentioned, in connection with the official carbonate, as the white pulverulent decomposition-product obtained when the official salt is exposed to air. It may be prepared either by treating official ammonium carbonate with twice its weight of water, when the carbamate will be dissolved, leaving the acid carbonate or bicarbonate; or the official salt may be kept for two weeks under a bell-glass over sulphuric acid and lime, when the carbamate will be decomposed into carbon dioxide and ammonia, which are absorbed by the acid and lime, leaving the bicarbonate as a friable mass. When perfectly dry, ammonium bicarbonate is free from ammoniacal odor; it is soluble in 8 parts of water at 15° C. (59° F.), but is insoluble in alcohol.

Ammonium Citrate. **$(NH_4)_3C_6H_5O_7$ or $C_3H_4(OH)(COONH_4)_3$.**—This may be prepared by neutralizing a solution of citric acid with ammonium carbonate or ammonia water and carefully evaporating the solution on a water-bath, adding a little ammonia water from time to time, as the salt is readily decomposed. 100 Gm. of citric acid require for neutralization either 76.75 Gm. of ammonium carbonate or 242.38 Gm. of 10 per cent. ammonia water, yielding 115.21 Gm. of a salt of the above composition.

Ammonium Phosphate. $(NH_4)_2HPO_4$. The British Pharmacopœia directs this salt to be prepared by adding stronger ammonia water to diluted phosphoric acid until a slight alkaline reaction ensues, then evaporating the solution with occasional addition of ammonia water and setting the liquid aside so that crystals may form, which must be quickly dried on paper.

Ammonium Sulphate. $(NH_4)_2SO_4$.—The crude salt is obtained by treating coal-gas liquor either with sulphuric acid or calcium sulphate; if the latter plan be followed, it is customary to percolate the gas-liquor through powdered gypsum, whereby ammonium sulphate is obtained in solution and calcium carbonate remains in the percolator. The solution is evaporated and crystallized, the crystals being purified by heating to about 240° C. (464° F.) to remove empyreumatic products, and final solution and recrystallization.

CHAPTER XLV.

THE COMPOUNDS OF CALCIUM AND STRONTIUM.

THE compounds of these two metals used in pharmacy are comparatively few in number, and may be conveniently grouped together. The Pharmacopœia recognizes 10 compounds of calcium and 6 preparations of the same, but only 3 compounds of strontium. The following list embraces all that are officially recognized:

Official English Name.	Official Latin Name.
Calcium Bromide,	Calcii Bromidum.
Precipitated Calcium Carbonate,	Calcii Carbonas Præcipitatus.
Prepared Chalk,	Creta Præparata.
Calcium Chloride,	Calcii Chloridum.
Calcium Hypophosphite,	Calcii Hypophosphis.
Precipitated Calcium Phosphate,	Calcii Phosphas Præcipitatus.
Dried Calcium Sulphate,	Calcii Sulphas Exsiccatus.
Lime,	Calx.
Lime Liniment,	Linimentum Calcis.
Chlorinated Lime,	Calx Chlorinata.
Sulphurated Lime,	Calx Sulphurata.
Solution of Lime,	Liquor Calcis.
Syrup of Lime,	Syrupus Calcis.
Syrup of Calcium Lactophosphate,	Syrupus Calcii Lactophosphatis.
Chalk Mixture,	Mistura Cretæ.
Compound Chalk Powder,	Pulvis Cretæ Compositus.
Strontium Bromide,	Strontii Bromidum.
Strontium Iodide,	Strontii Iodidum.
Strontium Salicylate,	Strontii Salicylas.

THE COMPOUNDS OF CALCIUM.

Calcium Bromide. $CaBr_2$.—The simplest method for the preparation of this salt is solution of calcium carbonate in hydrobromic acid, an excess of the former being added, the mixture filtered when effervescence has ceased, and the solution evaporated to dryness; a white granular powder is thus obtained, which is very deliquescent, and must be preserved in tightly stoppered bottles.

The Pharmacopæia demands not less than 97 per cent. purity for this salt, but gives no direction for determining the same, although tests are given for the absence of barium, calcium bromate, and iodides, and for the limit of nitrates and ammonia.

Precipitated Calcium Carbonate. $CaCO_3$.—This salt, popularly known as precipitated chalk, is prepared by double decomposition between calcium chloride and sodium carbonate; solutions of the two salts are mixed and heated, when calcium carbonate is thrown down as a dense precipitate, while sodium chloride remains in solution. The decomposition may be illustrated as follows: $CaCl_2 + Na_2CO_3 = CaCO_3 + 2NaCl$; to remove the sodium chloride, the mixture is poured on a strainer and the precipitate washed with boiling water until the washings no longer indicate the presence of chlorine.

If calcium carbonate be precipitated in the cold, it is flocculent and voluminous, in which condition it is difficult to wash it entirely free from the sodium chloride; hence the use of heat is advantageous. The precipitate consists of a micro-crystalline powder, entirely free, however, from grittiness.

It is not adapted for internal use, but is employed in the preparation of other calcium compounds.

Prepared Chalk. $CaCO_3$.—The compound officially recognized under the name prepared chalk is native soft calcium carbonate, freed by elutriation from most impurities. Chalk occurs abundantly, as a soft earthy mineral, on the English coast, which, by repeated treatment with water, may gradually be freed from impurities and coarser particles. The process of elutriation has been fully explained on page 114. After collecting the suspended fine powder, the latter, while still moist, is formed into small nodular masses by means of a funnel and then dried.

Chemically, prepared chalk does not differ from the precipitated calcium carbonate, but, on account of its greater softness and adhesiveness, it is better adapted for internal administration, and is the kind of chalk used in the official chalk mixture. Although it is never so white, and is probably less pure than the preceding article, the latter should never be used in its place.

Calcium Chloride. $CaCl_2$.—This compound is extensively obtained in a crude state as a by-product in different chemical processes. It may be obtained pure either by dissolving pure calcium carbonate in pure hydrochloric acid or by dissolving ordinary chalk or marble in hydrochloric acid and freeing the solution from iron and other impurities by treatment with chlorine and subsequently milk of lime; the mixture is warmed and filtered, the filtrate being finally exactly neutralized with hydrochloric acid.

If a concentrated solution of calcium chloride be set aside to crystallize, a salt of the composition $CaCl_2 + 6H_2O$, containing nearly 50 per cent. of water, will be obtained; but if the solution be evaporated until a granular powder results, a very deliquescent white salt of the composition $CaCl_2 + 2H_2O$, containing about 25 per cent. of water, is produced. The Pharmacopœia recognizes only the anhydrous salt, which requires for its preparation a temperature above 200° C. (392° F.), perfect fusion not occurring much below a red heat. The official salt is very deliquescent, and must be preserved in tightly stoppered bottles.

Anhydrous calcium chloride is employed in pharmacy chiefly as a desiccating agent, while the crystallized salt is used as a reagent in analytical chemistry.

Calcium Hypophosphite. $Ca(PH_2O_2)_2$.—This salt, the parent salt of numerous other hypophosphites, is prepared by the direct action of phosphorus on calcium hydroxide in the form of milk of lime, phosphine, or hydrogen phosphide, being generated at the same time; $3Ca(OH)_2 + 6H_2O + P_8 = 3Ca(PH_2O_2)_2 + 2PH_3$. In order to avoid, as far as possible, the formation of the very annoying and spontaneously inflammable phosphine, E. Scheffer, as early as 1858, advocated the use of partially oxidized phosphorus, prepared by treating it under water with atmospheric air, whereby the phosphorus is changed to a spongy condition and combines more readily with lime, even at the ordinary temperature, but preferably if the mixture be heated to 55° C. (131° F.). When the reaction has ended, the mixture is filtered, the residue washed with water, and the united filtrates evaporated and granulated or allowed to crystallize.

Calcium hypophosphite is not hygroscopic, like the corresponding salts of potassium and sodium, and is very nearly as soluble in cold as in boiling water. The Pharmacopœia requires that the salt shall contain not less than 98 per cent. of pure $Ca(H_2PO_2)_2$, which must be determined gravimetrically, as explained under Potassium Hypophosphite; the former volumetric determination with potassium permanganate being unreliable.

Precipitated Calcium Phosphate. $Ca_3(PO_4)_2$.—Tricalcium phosphate may be obtained by digesting calcined bone with hydrochloric acid, whereby acid calcium phosphate and calcium chloride are formed, both of which remain in solution, and upon addition of ammonia are converted into tricalcium phosphate and ammonium chloride, the former being precipitated and freed from the latter by repeated washing with water. The different steps in the process may be illustrated by the following equations: $Ca_3(PO_4)_2 + 4HCl = CaH_4(PO_4)_2 + 2CaCl_2$ and $CaH_4(PO_4)_2 + 2CaCl_2 + 4NH_4OH = Ca_3(PO_4)_2 + 4NH_4Cl + 4H_2O$. If the precipitation is effected in a cold solution, the resulting product will be more voluminous but less readily freed from accompanying impurities than if hot solutions are used. Precipitated calcium phosphate may also be obtained by adding a solution of calcium chloride and ammonia water to a solution of sodium phosphate, when the following reaction will occur: $3CaCl_2 + 2NH_4OH + 2Na_2HPO_4 = Ca_3(PO_4)_2 + 2NH_4Cl + 4NaCl + 2H_2O$.

The calcium phosphate of the German Pharmacopœia differs from that of the United States and British Pharmacopœias in being secondary calcium phosphate, $CaHPO_4$, obtained by decomposition of calcium chloride with sodium phosphate; it is a crystalline powder, containing about 25 per cent. of water, and has the formula $CaHPO_4 + 2H_2O$.

Dried Calcium Sulphate.—The terms dried gypsum and calcined plaster are also applied to this compound, which is obtained by carefully heating native crystalline calcium sulphate, or gypsum, $CaSO_4 + 2H_2O$, until deprived of about three-fourths of its water. The heat must be carefully regulated, and not allowed to exceed 105° C. (221° F.), as above this temperature the last portions of water will be expelled and the compound become anhydrous. If heated to 200° C. (392° F.), gypsum loses its property of uniting with water and setting to a firm mass, thus becoming useless for surgical purposes.

The official exsiccated calcium sulphate is a powder containing about 95 per cent. of calcium sulphate and 5 per cent. of water. It must be carefully protected from moisture.

Lime. CaO.—Calcium oxide, better known as unslaked or caustic lime, is obtained by calcining calcium carbonate in suitable furnaces known as lime-kilns. Oyster-shells, limestone, marble, and other varieties of calcium carbonate are used for the purpose, the final product varying in quality according to the source; for pharmaceutical and chemical purposes, lime obtained by calcination of white marble is the most desirable, being less contaminated with impurities.

Good lime occurs in hard but porous masses, which, upon addition of half their weight of water, become heated and are converted into a soft white powder, known as slaked lime. The change is of a chemical nature, as is evidenced by the development of heat, resulting in the formation of calcium hydroxide: thus, $CaO + H_2O = Ca(OH)_2$. Since lime, upon exposure to air, gradually absorbs moisture, and finally carbon dioxide, it must be preserved in well-closed vessels in a dry place. Lime thus changed by exposure is called air-slaked lime.

Lime is used in pharmacy as a dehydrating agent and for the preparation of the official solution and syrup of lime. When slaked and mixed with five or six times its weight of water it forms a mixture known as *milk of lime.*

Chlorinated Lime.—This compound, which owes its value entirely to the amount of available chlorine it contains, is prepared by exposing slaked lime on trays to the action of chlorine gas, care being taken that the temperature does not rise above 25° C. (77° F.), to avoid the formation of calcium chlorate. The views held by chemists regarding the nature of the compound formed differ, and the question has, at the present day, not been settled. Some contend that calcium hypochlorite, calcium chloride, and water are produced, according to the equation $2Ca(OH)_2 + Cl_4 = Ca(ClO)_2 + CaCl_2 + 2H_2O$, while others regard the dry product as having the composition $CaOCl_2$ or $CaCl(OCl)$, which, upon the addition of water, breaks up into calcium hypochlorite and chloride. The preponderance of opinion, at present, is in favor of the latter view, partly because the richest commercial samples of chlorinated lime or bleaching powder thus far produced do not contain the proportion of available chlorine (about 49 per cent.) which the compound $Ca(ClO)_2 + CaCl_2 + 2H_2O$ should yield.

The term "chloride of lime," usually applied to this substance in commerce, is a misnomer, probably given to it long before the chemical nature of the manufacturing process was understood.

Chlorinated lime always contains some calcium hydroxide, to which its partial insolubility in water is due. It should be kept in a cool, dry place, and protected from light, since the latter has a deleterious effect upon it, causing a loss of chlorine and oxygen, with production of calcium chlorate and chloride. If of good quality, chlorinated lime is not deliquescent, the latter phenomenon indicating decomposition.

Solutions of chlorinated lime should always be prepared, without heat, by triturating the powder in a mortar with successive portions of water and rapidly filtering through paper or cotton.

The Pharmacopœia requires that the official product shall contain at least 30 per cent. of available chlorine, which may be determined, as in the case of solution of chlorinated soda, by treatment with hydrochloric acid and potassium iodide and subsequent titration of the liberated iodine with sodium thiosulphate. When hydrochloric acid is added to chlorinated lime, the following decomposition takes place: $2Ca(ClO)Cl$ or $(Ca(ClO)_2 + CaCl_2) + 4HCl = Cl_4 + 2CaCl_2 + 2H_2O$. The action of nascent chlorine on potassium iodide has been explained on page 515, and, from the amount of $\frac{N}{10}$ sodium thiosulphate solution used to decolorize the iodine solution, the weight of liberated chlorine can be calculated. In the official test, between 3 and 4 Gm. of the sample are accurately weighed and then shaken with sufficient water to make 1000 Cc. of the mixture, of which 100 Cc., representing one-tenth of the original weight of chlorinated lime taken, are used for the assay. As each Cc. of the sodium thiosulphate solution required to decolorize the solution corresponds to 0.003518 Gm. of chlorine, the number used, when multiplied by 0.3518 (0.003518×100) and divided by the weight of chlorinated lime represented by the 100 Cc. of mixture taken, will express the percentage of available chlorine present.

Sulphurated Lime.—The official process for this preparation consists in heating a mixture of 70 parts of dried calcium sulphate, 10 parts of charcoal, and 2 parts of starch, in a loosely covered crucible, to bright redness until a uniform gray color results. The reaction consists in the reduction of calcium sulphate to sulphide and the formation of carbon monoxide and dioxide, which escape, thus: $CaSO_4 + C_3 = CaS + 2CO + CO_2$. The starch simply aids in the reduction, which, however, is not complete, as the finished product contains unchanged calcium sulphate and carbon in varying proportions.

Sulphurated lime, being liable to decomposition when exposed to air, must be carefully preserved in air-tight vessels. The official article is required to contain at least 60 per cent. of calcium monosulphide, upon which the virtues of the preparation depend; the determination being made by adding 1 Gm. of sulphurated lime to a boiling solution of 2.08 Gm. of crystallized cupric sulphate, when the copper should be completely precipitated as sulphide. The equation $CuSO_4.5H_2O + CaS = CuS + CaSO_4 + 5H_2O$ shows that 247.85 parts of crystallized cupric sulphate require 71.63 parts of calcium monosulphide; hence 2.08 Gm. will require 0.601 Gm., which is practically 60 per cent. of 1 Gm.

The official title does not appear to have been well chosen, and the name Calcii Sulphidum Venale, Commercial Calcium Sulphide, would convey a better idea of the character of the compound, especially as the official requirement is for not less than 60 per cent. of pure CaS, which in some samples has been found to run even as high as 70 per cent. and over.

Solution of Lime.—This liquid, more familiarly known as lime water, is intended to be a saturated solution of calcium hydroxide. The official directions for its preparation are simple and easily followed: a convenient quantity of lime having been slaked is mixed with 30 times its weight of water and frequently agitated during a half-hour; the liquid is decanted and thrown away, and to the residue is added about 300 times as much water as the weight of original lime used, and the mixture poured into bottles. The object of rejecting the first solution obtained after half an hour's maceration of the slaked lime with water is to get rid of the more soluble impurities, after which the purified lime is kept in contact with water as long as it continues to furnish a saturated solution. It must not be supposed, however, that even the best lime will furnish unlimited quantities of good lime water, and the supply should be tested from time to time, either volumetrically, as directed by the Pharmacopœia, or empirically, by breathing into a small quantity of it through a glass tube or boiling a little of it in a test-tube—in either case a turbid liquid should result, due to the separation of calcium carbonate in the first place, or calcium hydroxide in the second.

Lime water is a very important article in pharmacy, and should receive careful attention, as it is chiefly used as an antacid for infants. Pure lime, free from alum, should be used, and either distilled water or that which has been boiled and cooled. The supply of lime water should be kept in tightly corked bottles, in a cool place, as carbon dioxide is readily absorbed and heat is unfavorable to solution of the lime. Lime water is best decanted from the sediment—or, if filtered, this must be done under cover—the sediment should then be again well distributed in the liquid, by agitation, after the desired supply of solution has been withdrawn.

While a saturated aqueous solution of lime at 15° C. (59° F.) contains about 1.70 or 1.75 Gm. of calcium hydroxide in every liter, the official requirement of not less than 0.14 per cent. more nearly represents the average strength of good lime water. According to the equation $H_2SO_4 + Ca(OH)_2 = CaSO_4 + 2H_2O$, showing that 97.35 Gm. of the acid are capable of neutralizing 73.56 Gm. of calcium hydroxide, each Cc. of $\frac{N}{10}$ acid containing 0.0048675 Gm. of absolute H_2SO_4, used in the official test, corresponds to 0.007356 per cent. or 0.003678 Gm. of $Ca(OH)_2$, and 19 Cc. will indicate 0.007356 × 19 or 0.14 per cent.

Syrup of Lime.—This preparation contains a much larger proportion of lime in solution than lime water, owing to the presence of sugar, and is, therefore, preferred in some cases. It is said to have been used with good results as an antidote in cases of poisoning by carbolic acid. As stated on page 247, syrup of lime when freshly prepared contains about 3.2 Gm. of lime, CaO, in every 100 Cc. (about 16 grains in 1 fluidounce); as it absorbs carbon dioxide rapidly from the air, it must be carefully preserved, and when filtration is necessary, as in its preparation, covered funnels only should be used.

The saccharated solution of lime of the British Pharmacopœia is a similar preparation, but contains only about one-half as much calcium oxide in solution.

Syrup of Calcium Lactophosphate.—This syrup has been fully considered on page 247.

Among the non-official salts of calcium there is one deserving of special mention, as it has been used by physicians more or less frequently during the past six or eight years:

Calcium Glycerophosphate, **$CaC_3H_7O_2PO_4 + H_2O$** or **$C_3H_5(OH)_2CaPO_4 + H_2O$**.—[illegible]

THE COMPOUNDS OF STRONTIUM.

Strontium Bromide. $SrBr_2 + 6H_2O$.—This salt may be prepared by neutralizing diluted hydrobromic acid with pure strontium carbonate added in excess, filtering the mixture, and evaporating the solution until crystals begin to form. Upon cooling, the salt separates in crystals, which should be dried at a moderate heat.

Since pure strontium carbonate is difficult to obtain, the use of pure strontium hydroxide has been suggested instead, as the latter may be prepared readily from the nitrate by converting it into oxide by calcination and then slaking this with water, removing any barium and calcium present by further appropriate treatment with water.

The official salt contains about 30.4 per cent. of water of crystallization, and deliquesces rapidly upon exposure to air. It can be rendered anhydrous by heating to 120° C. (248° F.). The Pharmacopœia requires that the crystalline salt shall contain not less than 97 per cent. of pure strontium bromide, to be determined by titration with $\frac{N}{10}$ $AgNO_3$ solution. In the official test 0.5 Gm. of absolutely pure $SrBr_2$ would require 28.33 Cc. of the silver solution, and a like weight of pure strontium chloride would require 37.79 Cc.; hence each 0.0946 Cc. used in excess of 28.33 indicates 1 per cent. of chloride, and 1.07 (29.4 — 28.33) Cc. would represent 11.31 per cent. if strontium chloride be the only impurity present, which is entirely too large; but it must not be overlooked that calcium salts, if present, will also materially increase the quantity of silver solution required for complete precipitation. The lower limit allowed, 27.48 Cc., indicates 0.485 Gm. of the crystalline strontium bromide, or 97 per cent. Barium and calcium bromides may be present as impurities; for the former the Pharmacopœia prescribes a limit test, while the latter is ignored.

Strontium Iodide. $SrI_2 + 6H_2O$.—Like strontium bromide, this salt may be prepared either from pure strontium carbonate or hydroxide by solution in the respective acid, but, since solution of hydriodic acid is rather unstable, it should be freshly prepared for the purpose. The process is identical with that for the preceding salt.

Strontium iodide is also deliquescent, but contains less water of crystallization (24.05 per cent.) than the bromide. By exposure to air and light it is colored yellow, and must, therefore, be preserved in dark, amber-colored bottles.

The Pharmacopœia demands at least 98 per cent. purity for the crystallized salt. In the official test, 0.5 Gm. of the salt, dissolved in water, is precipitated by addition of an excess of $\frac{N}{10}$ $AgNO_3$ solution in the presence of nitric acid, the excess being determined by means of potassium sulphocyanate solution, using ferric ammonium sulphate as indicator. The Pharmacopœia requires that not less than 21.9 (25 — 3.1) nor more than 23.3 (25 — 1.7) Cc. of the silver solution shall be used, the 0.5 Gm. of salt used, if absolutely pure, requiring 22.42 Cc., and if containing 98 per cent. of SrI_2, 21.52 Cc. As, in the case of the preceding salt, the presence of barium will lower the quantity of silver nitrate solution necessary for complete precipitation, while the presence of calcium and of chlorides will increase the same.

Strontium Salicylate. $Sr(C_7H_5O_3)_2 + 2H_2O$ or $(C_6H_4(OH)COO)_2Sr + 2H_2O$.—This salt may be prepared by suspending 10 parts of salicylic acid in 100 parts of hot water and gradually adding 5.34 parts of strontium carbonate free from iron; when effervescence has ceased the solution is filtered and then allowed to crystallize, or it may be evaporated to dryness.

The Pharmacopœia requires 98.5 per cent. purity for this salt, which is determined gravimetrically by heating 0.5 Gm. of it with sulphuric acid in a crucible and finally igniting the newly formed sulphate until white and of constant weight; the residue of anhydrous strontium sulphate should weigh not less than 0.227 Gm. As 394.72 parts of pure crystallized strontium salicylate are capable of yielding 182.29 parts of anhydrous strontium sulphate, 0.5 Gm. if pure, should yield 0.230 + Gm., and if 98.5 per cent. pure at least 0.2265 Gm. should be obtained, which is practically 0.227 Gm.

CHAPTER XLVI.

THE COMPOUNDS OF MAGNESIUM.

ALTHOUGH the official magnesium salts are but few in number, they are extensively employed both by physicians and in domestic practice. The Pharmacopœia recognizes 6 preparations of magnesium, of which 1 is a liquid. The following comprise the list:

Official English Name.	Official Latin Name.
Magnesium Oxide (Magnesia),	Magnesii Oxidum.
Heavy Magnesia,	Magnesii Oxidum Ponderosum.
Magnesium Carbonate,	Magnesii Carbonas.
Magnesium Sulphate,	Magnesii Sulphas.
Effervescent Magnesium Sulphate,	Magnesii Sulphas Effervescens.
Solution of Magnesium Citrate,	Liquor Magnesii Citratis.

Magnesia. MgO.—The name calcined magnesia, by which this compound is commonly known, indicates the manner of its preparation. Magnesium carbonate is pressed somewhat firmly into a crucible and then heated to dull redness, whereby carbon dioxide and water are expelled, leaving about 42 per cent. of residue consisting of magnesium oxide. The process is known to be completed when a small quantity of the residue, suspended in water, no longer effervesces upon addition of an acid. The heat is not allowed to rise to full redness unless the powder can be kept constantly stirred, otherwise the magnesia is very apt to become granular. The following equation illustrates the change taking place: $4MgCO_3 + Mg(OH)_2 + 5H_2O = 5MgO + 4CO_2 + 6H_2O$.

Two varieties, a light and a dense calcined magnesia, occur in commerce; the latter is recognized in the Pharmacopœia as heavy magnesium oxide, or heavy magnesia. The two varieties are obtained in the same manner, but from light and heavy magnesium carbonate, respectively. Light magnesia is the kind generally used, and should invariably be employed when magnesia is to be dispensed in aqueous suspension; small quantities of water cannot be mixed with it without rendering it harsh and gritty, and, if 1 part of magnesia be added to 15 parts of water, the mixture will soon set to a gelatinous mass, hence care must be observed that sufficient water be used to overcome this tendency, and never should the water be added to the magnesia, but always the magnesia to the water. This peculiar behavior with water is due to the formation of gelatinous magnesium hydroxide, $Mg(OH)_2$, and is characteristic of light magnesia, heavy magnesia not readily uniting with water.

Light and heavy magnesia do not differ from each other chemically; the latter is a smoother and denser powder, preferred for use in powder mixtures on account of its smaller bulk.

The Pharmacopœia requires official magnesia to contain not less than 96 per cent. of pure magnesium oxide, to be determined by dissolving 0.4 Gm. of recently ignited and cooled magnesia in an excess, 25 Cc., of normal sulphuric acid and titrating the excess by means of normal KOH solution; not more than 5.8 Cc. of the latter should be required, showing that 19.2 Cc. of the acid have been used by the magnesia. As each Cc. of normal acid corresponds to 0.020003 Gm. of MgO, it represents 5 per cent. of the 0.4 Gm. taken for the test, and 19.2 Cc. will represent 96 per cent.

Since magnesia absorbs moisture and carbon dioxide readily from the air, it must be preserved in tightly closed tin or glass vessels. The Pharmacopœia demands that only slight traces of carbonate shall be present, and not more than 15 per cent. of water of hydration.

Magnesium Carbonate. $4MgCO_3 + Mg(OH)_2 + 5H_2O$.—As shown by the chemical formula, the official magnesium carbonate is not a pure normal carbonate, but is composed of magnesium carbonate and hydroxide united with water. It is prepared by mutual decomposition between solutions of magnesium sulphate or chloride, and of sodium carbonate; the composition of the resulting precipitate depends upon the concentration of the solutions employed, and the temperature at which the decomposition is effected and the precipitate dried. Pure normal magnesium carbonate is never obtained when a solution of the sulphate or chloride is mixed with an alkali carbonate, but always a basic carbonate, the proportion of normal carbonate present in the precipitate being greatest when dilute solutions are used at ordinary temperature.

If solutions of magnesium sulphate and sodium carbonate be mixed in the cold, no carbon dioxide is eliminated, a voluminous precipitate of basic magnesium carbonate being thrown down, while an acid magnesium carbonate, $MgH_2(CO_3)_2$, remains in solution; but if the solutions be mixed warm or hot, carbon dioxide is evolved. The reaction producing the official magnesium carbonate is probably as follows: $5(MgSO_4 + 7H_2O) + 5(Na_2CO_3 + 10H_2O) = (4MgCO_3 + Mg(OH)_2 + 5H_2O) + 5Na_2SO_4 + CO_2 + 79H_2O$, dilute solutions being used and mixed at a temperature not above 55° C. (131° F.); the precipitate is washed to remove sodium sulphate and dried without heat.

Both light and heavy magnesium carbonate occur in commerce, being manufactured extensively in this country and in England. The U. S. Pharmacopœia recognizes only the light variety, as indicated by the official description; this is also known as *magnesia alba*. It demands that official magnesium carbonate shall upon ignition yield not less than 40 per cent. of residue, of which not less than 96 per cent. shall consist of pure magnesium oxide. The British Pharmacopœia recognizes both the light and the heavy magnesium carbonate, and gives working formulas for their preparation, which differ from each other only in the concentration of the solutions used and in the length of time the mixture is boiled; the official English magnesium carbonate has the composition $3MgCO_3 + Mg(OH)_2 + 4H_2O$.

Considerable magnesium carbonate is also made in England from dolomite, a native magnesium limestone, by ignition and treatment with water and carbon dioxide under pressure; acid magnesium carbonate is formed and readily dissolved, and the solution, separated from the calcium carbonate, is treated with steam, whereby the basic carbonate is precipitated.

Magnesium Sulphate. $MgSO_4 + 7H_2O$.—This salt, better known as Epsom Salt (a name given to it in connection with its first production at Epsom, England, in 1695), may be made from native magnesium carbonate, magnesite, by treatment with diluted sulphuric acid, but is obtained on a more extensive scale from kieserite, a native magnesium sulphate, found near Stassfurt, in Germany. The mineral is first heated by itself and then treated with boiling water, whereby the magnesium sulphate is brought into solution, being subsequently purified by crystallization.

Magnesium sulphate contains 51.13 per cent. of water of crystallization, and slowly effloresces on exposure to dry air. The small acicular or rhombo-prismatic crystals, in which form it occurs in commerce, are produced by agitation of the crystallizing solution, whereby the formation of large crystals is prevented.

The Pharmacopœia demands an almost absolutely pure product, requiring that official magnesium sulphate shall contain not less than 99.7 per cent. of the crystallized salt.

Several natural purgative waters, known as bitter waters, owe their therapeutic properties to the magnesium sulphate which they contain.

The German Pharmacopœia directs the preparation of dried magnesium sulphate, for dispensing purposes, in powder-form. It is made by gradually heating crystallized magnesium sulphate on a water-bath until about two-thirds of the water has been expelled; the resulting white powder must be preserved in tightly corked bottles.

Effervescent Magnesium Sulphate.—This preparation, introduced into the Pharmacopœia to replace the former official effervescent magnesium citrate, represents about 50 per cent. of its weight of crystallized magnesium sulphate. The latter is deprived of its water of crystallization, by heating on a water-bath, before mixing it with the citric and tartaric acids and sodium bicarbonate. The granular compound is made by the general process directed in the Pharmacopœia for the preparation of all granular effervescent salts, and has already been considered in the chapter on Granular Effervescent Salts (see page 410).

Solution of Magnesium Citrate.—This popular preparation is directed to be made by first forming a solution of citric acid 33 Gm., magnesium carbonate 15 Gm., and water 120 Cc., and adding to it water 180 Cc., syrup of citric acid 60 Cc., and potassium bicarbonate 2.5 Gm., whereby the liquid is rendered effervescent and more agreeable in taste. The magnesium carbonate and citric acid are ordered in the proper proportions for the formation of acid magnesium citrate, which is more soluble, and therefore remains in solution better than the normal citrate. The equation $(4MgCO_3 + Mg(OH)_2 + 5H_2O) + 5(H_3C_6H_5O_7 + H_2O) = 5MgHC_6H_5O_7 + 4CO_2 + 16H_2O$ shows that 1 molecule or 482.26 Gm. of official magnesium carbonate requires 5 molecules or 1042.5 Gm. of citric acid; hence 15 Gm. will require 32.43 Gm.

When the solution is made up for stock, trouble sometimes arises from the use of plain water, and fungi have been met with in the finished product after the lapse of some time, which renders the preparation unsightly and unsalable. This may be overcome by boiling and filtering the water to be used. As retention in the solution of all carbon dioxide, from the potassium bicarbonate, adds materially to the refreshing taste, the bottles should be securely stoppered and kept in a cool place, lying on the side. Unless patent stoppers are attached to the bottles, sound, soft corks only should be used, and, having first been swelled in water for an hour, they should be driven firmly into the neck of the bottles and then secured with twine or wire.

In connection with the preceding magnesium compounds another may be considered, because of its use in pharmacy, which is officially recognized under the name Talcum. Commercial talc, which is defined as a native hydrous magnesium silicate, occurs of varying degrees of purity, but in its natural state is not suitable for pharmaceutical work, and hence the Pharmacopœia directs the preparation of a purified article for use as a filtering medium.

Talcum Purificatum. Purified Talc.—The official directions for preparing this filtering agent are intended to remove iron and such other impurities as may be soluble in the boiling water containing about 2 per cent. of hydrochloric acid. The treatment is repeated with a weaker acid, after which the insoluble residue is washed with water until all traces of the acid have been removed, and the purified talc is then dried at 110° C. (230° F.). When thus treated, purified talc should be entirely free from iron and upon ignition leave not less than 95 per cent. of residue. The limit of soluble substances allowed is fixed by the Pharmacopœia at 0.01 per cent., or 1 part in 10,000. Purified talc is an excellent filtering medium if used in powder of about No. 60, or at the utmost No. 80, fineness, but the bolted varieties used for dusting purposes are unsuitable, as they will pass through the filter paper.

CHAPTER XLVII.

THE COMPOUNDS OF ALUMINUM AND CERIUM.

THERE are but 4 compounds of aluminum and 1 of cerium recognized in the Pharmacopœia, as shown by the following list:

Official English Name.	Official Latin Name.
Alum,	Alumen.
Exsiccated Alum,	Alumen Exsiccatum.
Aluminum Hydroxide,	Alumini Hydroxidum.
Aluminum Sulphate,	Alumini Sulphas.
Cerium Oxalate,	Cerii Oxalas.

THE COMPOUNDS OF ALUMINUM.

Alum. $AlK(SO_4)_2 + 12H_2O$.—In pharmacy and medicine the term alum is applied to but one compound, although chemists recognize under the general name of alum several definite salts, the characteristics of which are that they are double sulphates of a univalent and trivalent element, are isomorphous, crystallizing in the regular system of the cube and octahedron, and contain 12 molecules of water of crystallization. The univalent elements present may be either potassium, sodium, ammonium, cæsium, rubidium, or silver, while the trivalent element need not necessarily be aluminum, its place being sometimes taken by iron, chromium, or manganese. The official alum is designated more specifically as potassium alum; besides this, the following are also known: ammonia alum, $AlNH_4(SO_4)_2 + 12H_2O$; chrome alum, $CrK(SO_4)_2 + 12H_2O$; iron alum, $FeNH_4(SO_4)_2 + 12H_2O$, etc.

Crude alum occurs in nature in the form of alunite or alumstone, a mixture of aluminum hydroxide and aluminum and potassium sulphates; from this, as well as from alum-shale and the minerals cryolite and bauxite, official alum is obtained. Calcination and lixiviation, as well as treatment with sulphuric acid and addition of potassium sulphate or chloride, are brought into requisition in the different processes, crystallization finally being employed for the purpose of purification. Owing to the presence of iron in the minerals from which alum is made, it is often found in the latter, but should not exceed traces, as determined by the official test with potassium ferrocyanide.

Potassium alum is not quite so soluble as ammonium alum, which latter was formerly recognized in the Pharmacopœia, and is still

Aluminum Sulphate. $Al_2(SO_4)_3 + 16H_2O$.—This salt is preferably prepared for medicinal purposes by dissolving freshly prepared aluminum hydroxide in a sufficient quantity of sulphuric acid properly diluted with water. An excess of acid should be avoided, as also an excess of the hydroxide; in the event of the latter, basic sulphates are likely to be formed. 100 Gm. of aluminum hydroxide (obtained from 607.45 Gm. of official alum) require 188.32 Gm. of absolute, or 203.58 Gm. of official, sulphuric acid to form a normal salt. The gelatinous hydroxide will dissolve quite readily, and the solution having been filtered is evaporated on a water-bath until a crystalline residue is obtained.

Aluminum sulphate contains about the same percentage of water of crystallization as official alum, but is far more soluble (about nine times) than the latter.

Besides the official aluminum compounds the following is sometimes used:

Solution of Aluminum Acetate.—This preparation is recognized in the German Pharmacopœia, and is prepared by adding 360 Gm. of 30 per cent. acetic acid to a solution of 300 Gm. of aluminum sulphate in 800 Cc. of water, and afterward introducing, in small portions at a time and with constant stirring, a mixture of 130 Gm. of calcium carbonate in 200 Cc. of water. The whole operation must be conducted in a cool place, and the mixture set aside for twenty-four hours, being stirred occasionally, when the clear liquid may be removed with the aid of a siphon. The solution contains about 7.5 or 8 per cent. of basic aluminum acetate of the composition $Al_2(OH)_2(C_2H_3O_2)_4$. The reaction taking place in the foregoing process may be illustrated thus: $(Al_2(SO_4)_3 + 16H_2O) + 4HC_2H_3O_2 + 3CaCO_3 = Al_2(OH)_2(C_2H_3O_2)_4 + 3CaSO_4 + 3CO_2 + 17H_2O$.

THE COMPOUNDS OF CERIUM.

Cerium Oxalate.—The official cerium oxalate is defined to be a mixture of the oxalates of cerium, didymium and lanthanum, together with oxalates of other rare earths of this group, and hence no chemical formula is given for the salt. The impurities are of course present in very small proportions and in no way affect the therapeutic value of the compound. The process for obtaining cerium oxalate from the mineral cerite, its chief source, is somewhat complicated. The powdered mineral is digested with sulphuric acid, the mass dried and treated with diluted nitric acid and hydrogen sulphide, to remove copper and other metals. The cerite metals are next precipitated by means of oxalic acid and the mixed oxalates, after the addition, of magnesium carbonate, are calcined and the residue dissolved in a small quantity of concentrated nitric acid. The solution is poured into a large quantity of water containing about 0.5 per cent. of sulphuric acid, whereby the cerium is precipitated as yellow ceric sulphate, while lanthanum and didymium, together with the magnesium, remain in solution. The ceric sulphate is dissolved in sulphuric acid and reduced to cerous sulphate, by means of sodium thiosulphate, after which it is precipitated, as cerous oxalate, with oxalic acid and dried. Cerium oxalate may also be readily obtained by interaction between a soluble cerium salt (nitrate) and a soluble oxalate.

Cerium oxalate, as a rule, occurs as a white, granular powder, but sometimes has a pink color, due to the presence of larger proportions of didymium. When heated to redness it is decomposed, leaving about 47 per cent. of a reddish-brown residue, consisting of ceric and other rare earth oxides. When pure, it has the formula $Ce_2(C_2O_4)_3 + 10H_2O$, as shown by Power and Sheddon.

Among the non-official salts of cerium, the nitrate, $Ce(NO_3)_3 + 6H_2O$, has been used to some extent. It may conveniently be made by decomposing cerous sulphate with barium nitrate, and possesses the advantage of being freely soluble in water and alcohol.

CHAPTER XLVIII.

THE COMPOUNDS OF IRON.

THERE is no class of inorganic compounds, excepting the official preparations of the alkalies, more extensively employed in medicine than those of iron; they must therefore be considered as among the most important in the study of pharmacy. The Pharmacopœia recognizes, besides iron in the metallic form, no less than 30 different preparations of the same, of which 9 are liquid. Chemists have grouped all compounds of iron into two classes, designated as ferrous and ferric compounds, respectively, which differ from each other in striking physical and chemical properties; this distinction has also been maintained in the official titles of the iron salts and their solutions. Ferrous compounds, in which iron is bivalent, are, when not anhydrous, of a green color, with one exception, the yellow oxalate, and form a blue precipitate of ferrous ferricyanide, $Fe_3(Fe(CN)_6)_2$, known as Turnbull's Blue, with solution of potassium ferricyanide; ferric compounds, in which iron is trivalent, on the other hand, are characterized by a reddish- or yellowish-brown color and form a blue precipitate of ferric ferrocyanide, $Fe_4(Fe(CN)_6)_3$, known as Prussian Blue, with solution of potassium ferrocyanide.

The following is a list of the official preparations of iron, divided, for convenience, into three classes:

Official English Name.	Official Latin Name.
Metallic Iron.	
Iron,	Ferrum.
Reduced Iron,	Ferrum Reductum.
Ferrous Compounds.	
Ferrous Sulphate,	Ferri Sulphas.
Exsiccated Ferrous Sulphate,	Ferri Sulphas Exsiccatus.
Granulated Ferrous Sulphate,	Ferri Sulphas Granulatus.
Mass of Ferrous Carbonate,	Massa Ferri Carbonatis.
Saccharated Ferrous Carbonate,	Ferri Carbonas Saccharatus.
Pills of Ferrous Carbonate,	Pilulæ Ferri Carbonatis.
Pills of Ferrous Iodide,	Pilulæ Ferri Iodidi.
Syrup of Ferrous Iodide,	Syrupus Ferri Iodidi.
Compound Iron Mixture,	Mistura Ferri Composita.
Ferric Compounds.	
Ferric Ammonium Sulphate,	Ferri et Ammonii Sulphas.
Ferric Chloride,	Ferri Chloridum.
Ferric Citrate,	Ferri Citras.

Official English Name.	Official Latin Name.
Ferric Compounds.—(Continued.)	
Ferric Hydroxide,	Ferri Hydroxidum.
Ferric Hydroxide with Magnesium Oxide,	Ferri Hydroxidum cum Magnesii Oxido.
Ferric Hypophosphite,	Ferri Hypophosphis.
Iron and Ammonium Citrate,	Ferri et Ammonii Citras.
Iron and Ammonium Tartrate,	Ferri et Ammonii Tartras.
Iron and Potassium Tartrate,	Ferri et Potassii Tartras.
Iron and Quinine Citrate,	Ferri et Quininæ Citras.
Soluble Iron and Quinine Citrate,	Ferri et Quininæ Citras Solubilis.
Iron and Strychnine Citrate,	Ferri et Strychninæ Citras.
Soluble Ferric Phosphate,	Ferri Phosphas Solubilis.
Soluble Ferric Pyrosphosphate,	Ferri Pyrophosphas Solubilis.
Solution of Ferric Chloride,	Liquor Ferri Chloridi.
Solution of Ferric Subsulphate,	Liquor Ferri Subsulphatis.
Solution of Ferric Sulphate,	Liquor Ferri Tersulphatis.
Solution of Iron and Ammonium Acetate,	Liquor Ferri et Ammonii Acetatis.
Tincture of Ferric Chloride,	Tinctura Ferri Chloridi.
Bitter Wine of Iron,	Vinum Ferri Amarum.
Wine of Iron,	Vinum Ferri.

Iron. Fe.—The kind of metallic iron recognized in the Pharmacopœia is that occurring in the form of soft, bright wire. It should be free from rust, and the commercial article, as it has usually been coated with grease or paraffin oil to protect it from moisture, must be thoroughly cleaned before it is used for pharmaceutical purposes. The kind of iron wire known in the trade as card-teeth, obtained as clippings and waste from the manufacturers of cotton cards, is usually preferred on account of its convenient form and general good quality; sometimes, however, card-teeth of a very inferior grade are sold, and require careful garbling and subsequent washing to remove grease and dirt.

Reduced Iron.—This preparation represents more or less pure metallic iron in a state of fine division, obtained by reduction of ferric oxide with hydrogen gas. Ferric hydroxide is first dried, whereby it is changed to oxyhydrate, and then placed in an iron reduction tube so arranged that the same can be heated to dull redness, while a current of hydrogen gas, previously washed and dried by being passed through a moderately strong solution of potassium permanganate and afterward sulphuric acid, is constantly passed through it. The reducing action of hydrogen on ferric oxide may be illustrated by the following equation: $Fe_2O_3 + H_6 = Fe_2 + 3H_2O$. The supply of hydrogen is kept up as long as any oxygen is left, as shown by the escape of aqueous vapor from the tube. When reduction is complete, the tube and contents are allowed to cool slowly, while a slow stream of hydrogen is continued until the temperature has been reduced to that of the air; this is necessary, otherwise the hot, finely divided iron will be readily reoxidized by the air, as in that condition its avidity for oxygen is very marked.

The quantity of reduced iron depends, of course, upon the purity of the ferric hydroxide and the temperature employed. When ferric oxide is heated to 280° or 300° C. (536°–572° F.) in a stream of hydrogen, it is converted into ferroso-ferric oxide, Fe_3O_4, $3Fe_2O_3 + H_2 = 2Fe_3O_4$ or $2(FeO + Fe_2O_3) + H_2O$, but metallic reduction does not occur until a temperature of 400° C. (752° F.) and over is reached. A bright-red heat, however, is not employed, as it causes a dense, compact product, which is not desirable; therefore the commercial article, although a lighter powder, is usually contaminated with imperfectly reduced oxide.

Reduced iron should be free from lustre and of a grayish color, and when treated with warm diluted sulphuric or hydrochloric acid should leave not more than 1 per cent. of insoluble residue. Its value is based upon the proportion of metallic iron present; the U. S. and German Pharmacopœias both demand 90 per cent., while the British Pharmacopœia admits reduced iron of 75 per cent. purity. Frequent examinations of the commercial products have disclosed the fact that much inferior reduced iron is dispensed by pharmacists, but few samples coming up to the official requirements.

The Pharmacopœia directs that the valuation of reduced iron shall be made by the iodometric method, which consists in adding an accurately weighed quantity of iodine, known to be in excess, to a given weight of reduced iron, in the presence of potassium iodide solution, and after maceration for one hour titrating the excess of iodine with sodium thiosulphate solution. The potassium iodide acts merely as a solvent for the iodine in the aqueous fluid, and thus brings the same into intimate contact with the iron. Since 251.8 Gm. of iodine are capable of combining with 55.5 Gm. of pure metallic iron, as shown by the equation $Fe + I_2 = FeI_2$, 0.01259 Gm., the amount of iodine represented by 1 Cc. of $\frac{N}{10}$ sodium thiosulphate solution will combine with 0.002775 Gm. of iron, which is exactly $\frac{1}{2}$ per cent. of the 0.555 Gm. taken for the assay, and 0.02518 Gm. of iodine, represented by 2 Cc. of the thiosulphate solution, will combine with 0.00555 or 1 per cent. of pure iron; hence the quotient obtained by dividing 2.6 by 0.02518 will express the percentage of pure iron corresponding to the 2.6 Gm. of iodine taken. If all the iodine taken could combine with the 0.555 Gm. of reduced iron there would be no necessity for further calculation, but as an unknown excess of iodine has been intentionally used, the exact amount in combination must be determined. Each Cc. of the sodium thiosulphate solution, as stated above, corresponds to $\frac{1}{2}$ per cent. of pure metallic iron in the 0.555 Gm. of reduced iron used, but as only $\frac{1}{4}$ of the excess of iodine is titrated in the 25 Cc. solution, the total excess is equivalent to 4 times the number of Cc. of the sodium thiosulphate solution used, and hence the percentage of pure metallic iron corresponding to such total excess of iodine must be represented by 4 times the number of Cc. of the thiosulphate solution required multiplied by $\frac{1}{2}$, or, in other words, by the number of Cc. multiplied proportion of 0.65 Gm. for 1 Gm. (or 6.5 grains for 10 grains) of the latter.

Granulated Ferrous Sulphate. $FeSO_4 + 7HO_2$.—This salt differs from official ferrous sulphate in being in the form of a crystalline powder instead of large crystals, containing, however, the same amount of water. It is of a much paler color than the crystals, and, owing to its mode of preparation, is less liable to oxidation. The washing of the crystalline powder with alcohol is for the purpose of removing the acid and uncombined water as completely as possible, thus facilitating drying; a more effectual plan is to pour the acid solution, when cold, into one-half its volume of alcohol, whereby the salt is precipitated and can then be drained on a strainer and washed with diluted alcohol until free from acid. Rapid drying in direct sunlight is advantageous, as it prevents oxidation.

Granulated ferrous sulphate presents a convenient form for dispensing purposes.

Mass of Ferrous Carbonate.—This preparation has been considered on page 368, which see.

Saccharated Ferrous Carbonate.—Although but little used at the present time, this preparation is still recognized in the Pharmacopœia. It closely resembles the preceding preparation except that it occurs in powder-form, and is directed to contain a minimum limit of ferrous carbonate. The official directions are to pour a hot solution of 50 Gm. of ferrous sulphate into a warm solution of 35 Gm. of sodium bicarbonate contained in a flask, aiding decomposition by rotating the vessel. The precipitate is repeatedly washed with hot water until the newly formed sodium sulphate has been removed, after which the precipitate is drained, mixed with 80 Gm. of sugar, evaporated to dryness, reduced to powder, and incorporated with sufficient sugar to make the finished product weigh 100 Gm. The reaction occurring between the ferrous sulphate and sodium bicarbonate may be seen from the following equation: $(FeSO_4 + 7H_2O) + 2NaHCO_3 = FeCO_3 + Na_2SO_4 + CO_2 + 8H_2O$. As the powder readily oxidizes if exposed to air, it must be preserved in tightly stoppered bottles.

The Pharmacopœia requires the presence of at least 15 per cent. of ferrous carbonate, determined by dissolving 1.15 Gm. of the powder in diluted sulphuric acid and titrating with potassium permanganate. Ferrous sulphate is formed, and the subsequent reaction is identical with that already explained under that head. Each Cc. $\frac{N}{10}$ $KMnO_4$ solution, corresponding to 0.027601 Gm. of crystallized ferrous sulphate, must be equivalent to 0.011505 Gm. of ferrous carbonate, for 1 molecule or 276.01 Gm. of the former salt yields 1 molecule or 115.05 Gm. of the latter. In the official test not less than 15 Cc. of the permanganate solution will be required to show at least 15 per cent. of $FeCO_3$, for each Cc. corresponds to 0.0115 Gm. or 1 per cent. of 1.115 Gm. taken.

Compound Iron Mixture.—This preparation has been considered on page 338 (which see). When freshly made, each Cc. contains about 0.0025 Gm. of ferrous carbonate (about 1.14 grains in each fluidounce).

Syrup of Ferrous Iodide.—This preparation, as stated on page 248, is a saccharine solution of ferrous iodide containing 5 per cent. of the latter compound. The first step in its manufacture is to obtain a solution of ferrous iodide by allowing iodine to act on an excess of metallic iron in the form of wire. The two elements combine in part, with the development of heat, forming some ferrous iodide which enables the remaining iodine to go into solution, and gradually all iodine is taken up by the iron, the color of the liquid changing to pale green. After heating the liquid to the boiling-point, a small quantity of sugar is dissolved therein to prevent oxidation of the ferrous iodide solution and the liquid then filtered, the remaining iron wire and flask being rinsed with hot water, which is also passed through the filter. The balance of the sugar is then dissolved in the filtrate by means of heat. Syrup of ferrous iodide, if unprotected, readily becomes oxidized when in contact with air, as shown by the formation of a dark color on the surface, gradually spreading downward, and as this can be prevented by the presence of reducing agents, the Pharmacopœia directs that a small proportion of diluted hypophosphorous acid shall be added before the final weight of finished syrup is made up by addition of distilled water, which was first suggested by Judge in 1855, and has been found superior to all other preservatives proposed.

The valuation of syrup of ferrous iodide is made volumetrically by means of $\frac{N}{10}$ silver nitrate solution, silver iodide being precipitated and ferrous nitrate remaining in solution. In the official test, 15.4 Cc. of a diluted syrup of ferrous iodide, representing 1.54 Gm. of the original syrup, are diluted with water, and an excess, 6 Cc., of the silver solution added together with some diluted nitric acid, and ferric ammonium sulphate test-solution as indicator. When precipitation has ceased, $\frac{N}{10}$ potassium sulphocyanate solution is added to determine the excess of silver solution present. Not more than 1 Cc. of the sulphocyanate solution should be required to precipitate the remaining silver nitrate as white silver sulphocyanate, to show that 5 Cc. of the silver solution have been required for precipitation of the 1.54 Gm. of syrup of ferrous iodide. The equation $2AgNO_3 + FeI_2 = 2AgI + Fe(NO_3)_2$ shows that 1 molecule or 307.3 Gm. of ferrous iodide requires 2 molecules or 337.38 Gm. of silver nitrate, and as each Cc. of the $\frac{N}{10}$ $AgNO_3$ solution contains 0.016869 Gm. of silver nitrate, it is capable of precipitating 0.015365 Gm. of ferrous iodide, and consequently corresponds to 1 per cent.

of the 1.54 Gm. of syrup taken for the test; hence 5 Cc. will indicate 5 per cent. As already explained under Strontium Iodide, the addition of nitric acid in the official test prevents discoloration of the liquid by the iron, and is always employed when silver nitrate is titrated with potassium sulphocyanate with ferric alum as an indicator.

Ferric Ammonium Sulphate. $FeNH_4(SO_4)_2 + 12H_2O$.—This salt, resembling ordinary alum somewhat in chemical constitution, is obtained by dissolving ammonium sulphate in a boiling solution of ferric sulphate and setting the liquid aside to crystallize. If a slight addition of sulphuric acid be made to the solution the crystals obtained will be more perfect in form and color.

The crystals are liable to deterioration on exposure to air and heat, hence they should be preserved in tightly stoppered bottles in a cool place; when recently obtained or carefully preserved, they are of a beautiful pale-violet or hyacinthine color, but their solution in water is of a brownish-yellow color gradually changing to red, and deposits a basic salt.

Ferric ammonium sulphate, also known as ferric alum or ammonio-ferric alum, should contain in the uneffloresced condition 99.5 per cent. of pure ferric ammonium sulphate, representing not less than 11.5 per cent. of metallic iron. The latter is determined by the iodometric method, involving the decomposition of potassium iodide by ferric chloride and titration of the liberated iodine by means of sodium thiosulphate. The addition of hydrochloric acid, as directed by the Pharmacopœia in the official test, converts the ferric sulphate into ferric chloride, which then in turn reacts with the potassium iodide added, as shown by the following equation: $(FeNH_4(SO_4)_2 + 12H_2O) + 4HCl = FeCl_3 + NH_4Cl + 2H_2SO_4 + 12H_2O$; $FeCl_3 + KI = I + KCl + FeCl_2$; from which it is seen that each atom or 125.9 Gm. of iodine liberated corresponds to 1 molecule or 478.69 Gm. of crystallized ferric ammonium sulphate and at the same time to 1 atom or 55.5 Gm. of metallic iron. Now, since each Cc. of $\frac{N}{10}$ sodium thiosulphate solution represents 0.01259 Gm. of iodine, it must correspond to 0.047869 Gm. of official ferric ammonium sulphate or 0.00555 Gm. of metallic iron, which latter figure is equal to 1 per cent. of the 0.555 Gm. of crystallized salt taken for the test, and hence 11.5 Cc. will be required to indicate 11.5 per cent. This same quantity of $\frac{N}{10}$ sodium thiosulphate solution will also indicate the purity officially demanded for $11.5 \times 0.047869 = 0.5505$, and 99.5 per cent. of 0.555 is 0.5522.

Ferric Chloride.—The pharmacopœial directions for the preparation of this compound are to evaporate official solution of ferric chloride on a water-bath to 40 per cent. of its weight and then set aside in a covered vessel so as to form a crystalline mass. The resulting product will contain about 73 per cent. of anhydrous ferric chloride and about 27 per cent. of water, and corresponds very nearly to the formula $FeCl_3 + 3H_2O$; but since ferric chloride will combine with different proportions of water under varying conditions, the Pharmacopœia gives no formula for the compound. Ferric chloride occurs in orange-yellow crystalline lumps, which are very deliquescent in moist air and must be preserved in tightly stoppered bottles protected from light, since, upon exposure to the latter, it is gradually reduced to ferrous chloride.

The Pharmacopœia requires that ferric chloride shall contain at least 22 per cent. of metallic iron in combination, which is determined volumetrically by allowing the ferric chloride to act upon potassium iodide and titrating the liberated iodine with sodium thiosulphate. In the official test the 55.5 Cc. of solution taken will contain 0.555 Gm. of ferric chloride. As shown in the preceding article each molecule of ferric chloride will liberate 1 atom of iodine, and each Cc. of the sodium thiosulphate solution corresponds to 1 per cent. of 0.555 Gm. of metallic iron; hence 22 Cc. will be required to indicate 22 per cent.

Ferric Citrate.—This compound, belonging to the class of scale salts of iron, is prepared by dissolving freshly prepared and well-washed ferric hydroxide in water with the aid of citric acid, concentrating the solution on a water-bath to a syrupy consistence, and spreading on plates of glass, which are then placed in warm dust-proof drying closets so that a part of the moisture may evaporate and the product be obtained in the form of scales. A temperature exceeding 60° C. (140° F.) should not be employed for scaling the salt, otherwise the latter will be slowly reduced to a ferrous compound. The usual yield is from 42 to 44 per cent. of the weight of solution evaporated, and failure to obtain perfect scales may be due to insufficient concentration of the liquid before spreading it on glass or to too high a temperature in drying.

Although all scale salts of iron contain water of hydration, the amount present varies, not only for different salts, but also for different lots of the same salt, and is dependent upon the temperature employed in scaling, subsequent exposure, etc.; no definite formula expressing the composition of the scale salts of iron, therefore, can be given. Carefully prepared ferric citrate was found by F. B. Power to contain 31.9 per cent. of water, which would correspond very nearly to the formula $FeC_6H_5O_7 + 6H_2O$, while some commercial samples contained but 8.4 and 15.2 per cent. In estimating the water of hydration, a temperature of 100° C. (212° F.) should not be exceeded, as, beyond this temperature, decomposition of the salt is likely to occur.

Ferric citrate is slowly but completely soluble in cold water, and for purposes of solution the so-called soluble citrate of iron (see Iron and Ammonium Citrate) is therefore preferable, but the plain ferric citrate should always be used for pill-masses and similar purposes.

The Pharmacopœia directs that the iron present in the various scale salts of iron shall be determined by the iodometric method, as explained in the case of ferric ammonium sulphate, the respective iron salts being first converted into ferric chloride by digestion with hydrochloric acid. In the case of ferric citrate the equivalent of 16 per cent. of metallic iron is demanded.

Ferric Hydroxide. **$Fe(OH)_3$.**—The official directions for making this compound are to pour 10 volumes of solution of ferric sulphate into 13.8 volumes of 10 per cent. ammonia water, both liquids having been previously largely diluted with water. The process should not be reversed, otherwise basic ferric sulphate may be formed. Large dilution with water and a cool temperature are essential to insure the precipitation of a fully hydrated oxide, as indicated by the above formula. Ammonia water is purposely used in excess, so as to insure complete decomposition of the ferric sulphate; the reaction occurring is as follows: $Fe_2(SO_4)_3 + 6NH_4OH = 2Fe(OH)_3 + 3(NH_4)_2SO_4$.

The bulky precipitate subsides very slowly, and must be repeatedly washed with cold water until the reaction for the presence of sulphates ceases and the odor of ammonia has disappeared. It is finally drained on a well-wetted strainer and mixed with sufficient cold water to make the weight of the finished product 3000 Gm. for every liter of solution of ferric sulphate used. In this condition the ferric hydroxide keeps fairly well for a time, if heat and light be excluded; but it gradually undergoes change, being converted into the compound $Fe_2O_2(OH)_2$, of a more decided reddish tint, and is then no longer suitable as an antidote, having lost its power to combine with weak acids.

Ferric hydroxide, freshly precipitated, is used in the preparation of certain official iron solutions.

Ferric Hydroxide with Magnesium Oxide.—This preparation is to be much preferred to the preceding as an antidote in cases of poisoning by arsenic, as it can be made available at very short notice, not requiring tedious manipulation. It consists of a mixture of ferric and magnesium hydroxides suspended in a dilute solution of magnesium sulphate, and is made by adding a dilute solution of ferric sulphate to a dilute mixture of calcined magnesia and water; the mixture is well shaken and is then ready for use.

The Pharmacopœia, with the view of economizing time in cases of emergency, recommends that the dilute solution of ferric sulphate and the mixture of magnesia and water be always kept on hand, ready for immediate use. The former consists of 40 Cc. of the official solution of ferric sulphate and 125 Cc. of water; the latter, of 10 Gm. of calcined magnesia added to 750 Cc. of water.

Ferric Hypophosphite. **$Fe(PH_2O_2)_3$.**—This salt can be conveniently prepared by a method proposed by F. X. Moerk, which consists in placing 30 Gm. of calcium hypophoshite in a flask with 100 Cc. of distilled water, and adding gradually 64.52 Gm. of the official ferric chloride solution, shaking well after each addition. The mixture is allowed to stand for three days, with frequent agitation, then filtered and washed until all calcium has been removed. The yield by this method is large and the product fully up to the official requirements.

It was at one time suggested that ferric hypophosphite could be made by mixing solutions of calcium hypophosphite and ferrous sulphate, removing the precipitated calcium sulphate by filtration, and evaporating the solution of ferrous hypophosphite to dryness. It was supposed that the ferrous salt was, by oxidation during the evaporation, converted into ferric hypophosphite; but instead of the normal salt a basic hypophosphite, $Fe_2O(PH_2O_2)_4$, is obtained, for want of a sufficiency of acid, as is similarly the case with the official solution of ferric subsulphate. Double decomposition of solutions of ferric sulphate or chloride and sodium hypophosphite is also impracticable, as the freshly precipitated ferric hypophosphite has been found somewhat soluble in water; thus loss would be entailed during the necessary washing of the precipitate.

Ferric hypophosphite dissolves readily in a warm, strong solution of an alkali citrate, and, in this form, is used in the preparation of certain syrups.

The Pharmacopœia requires the official salt to contain 98 per cent. of absolute $Fe(PH_2O_2)_3$, which must be determined gravimetrically by a somewhat tedious process, since volumetric determination by means of potassium permanganate has been found unreliable, as already explained under Potassium Hypophosphite.

Ferric Phosphate, Soluble.—The official phosphate of iron, which occurs in scale form and is soluble in water, must not be confounded with the insoluble commercial article of a similar name. The latter is a slate-colored powder of variable composition, consisting of a mixture of insoluble ferrous and ferric phosphates, obtained by precipitation of a solution of ferrous sulphate by means of sodium phosphate and drying the resulting product.

Soluble ferric phosphate may be made by adding 11 parts of crystallized sodium phosphate to a solution of 10 parts of ferric citrate in twice its weight of water, evaporating the resulting green-colored solution, at a temperature not exceeding 60° C. (140° F.), to a syrupy consistence and spreading the same on glass plates, as in the case of ferric citrate. It is important that uneffloresced sodium phosphate be used to avoid an excess of this salt, which would cause the scales to become opaque and white on standing. The salt should be preserved in tightly corked bottles, in a dark place, otherwise its color will gradually darken and its solubility be impaired.

The exact composition of this salt cannot be stated, as it may be a mixture of ferric phosphate and sodium citrate, or possibly a mixture of four salts, ferric and sodium phosphates and ferric and sodium citrates, incomplete decomposition having taken place; hence the name sodio-citrophosphate of iron is frequently applied to the preparation.

The Pharmacopœia requires that soluble ferric phosphate shall contain iron in combination corresponding to 12 per cent. of that metal, which is determined as in the case of Ferric Citrate.

Ferric Pyrophosphate, Soluble.—This preparation closely resembles the preceding compound, and may be made in a similar manner, except that sodium pyrophosphate is used in place of the phosphate, and that the sodium and iron salts are used in equal proportions. Formerly this preparation was made by precipitating a white ferric pyrophosphate, $Fe_4(P_2O_7)_3$, from a solution of ferric sulphate by means of sodium pyrophosphate, dissolving this precipitate in solution of sodium or ammonium citrate and concentrating and scaling the solution so obtained.

The composition of soluble ferric pyrophosphate is as uncertain as that of the preceding scale salt, hence no definite formula as to its constitution can be given. Like the soluble ferric phosphate, it must be carefully protected against exposure to air and light. The two preparations are both of a green color (the phosphate bright green, the pyrophosphate apple green), but may readily be distinguished from each other by boiling some of the salt with sodium hydroxide solution, filtering, acidulating the filtrate with hydrochloric acid, and adding some magnesia test mixture (see U. S. Pharmacopœia) and a slight excess of ammonia water; in the case of the phosphate a white crystalline precipitate of ammonium magnesium phosphate, NH_4MgPO_4, will occur, while the solution of the pyrophosphate will not be disturbed at all.

Although ferric pyrophosphate in scales is known in commerce simply as pyrophosphate of iron, it is always best to designate it as soluble pyrophosphate of iron, because the true ferric pyrophosphate also occurs on the market (although rarely) in the form of a white insoluble powder.

The amount of iron present in this preparation is required by the Pharmacopœia to be equivalent to 10 per cent. of metallic iron. The method of determination is identical with that designated for the other scale salts of iron.

Iron and Ammonium Citrate.—This preparation resembles the official ferric citrate in appearance, but is more readily soluble than it in cold water. It is obtained by mixing 100 Cc. of a 50 per cent. solution of ferric citrate with 40 Cc. of 10 per cent. ammonia water, concentrating and scaling the solution exactly as in the case of ferric citrate. The resulting product must of necessity be of variable composition, both as regards the amount of water of hydration and also the relative proportions of ferric and ammonium citrates present.

The official title, iron and ammonium citrate, would indicate a true double salt, which, when anhydrous, should be of uniform composition; such is not the case, however, and, as the Pharmacopœia requires the compound to contain exactly the same relative amount of iron, 16 per cent., as the plain ferric citrate, there cannot be much ammonium citrate present. The name soluble ferric citrate appears more appropriate, and serves to distinguish it from the less soluble article. Inasmuch as ferric citrate is very rarely used in any other form than that of solution, it seems superfluous to have two preparations so nearly identical and differing from each other chiefly in degree of solubility.

Iron and ammonium citrate is more hygroscopic than ferric citrate, and upon exposure to air rapidly loses ammonia and becomes less soluble, hence it must be preserved in tightly stoppered bottles; light also has a deleterious effect upon it. If at any time the scale salt has suffered by age or careless exposure, ready solution can usually be effected by the cautious addition of a drop or two of ammonia water to the residue.

Iron and Ammonium Tartrate.—In the manufacture of this scale salt the first step is the preparation of ferric hydroxide from solution of ferric sulphate, which has been explained on page 555; the next step is to make a solution of acid ammonium tartrate by neutralizing a solution of tartaric acid exactly with ammonia water and adding to this another like weight of tartaric acid. The well-washed ferric hydroxide is then added in successive portions to the solution of acid ammonium tartrate and dissolved with the aid of a moderate heat, after which the solution is treated as in the case of the other scale salts of iron.

The reaction occurring may be illustrated by the following equation: $Fe(OH)_3 + NH_4HC_4H_4O_6 = NH_4(FeO)C_4H_4O_6 + 2H_2O$, in which the group FeO, to which the name ferryl has been given, acts as a univalent radical, like antimonyl. The scale compound when carefully deprived of all water probably has the composition expressed by the formula $NH_4(FeO)C_4H_4O_6$ or $(CHOH)_2COONH_4\text{-}COO(FeO)$.

Iron and ammonium tartrate is a deliquescent compound, requiring the careful exclusion of air and light. Like iron and ammonium citrate, it is prone by age and exposure to become acid in character, and will then need the careful addition of a little ammonia water to restore neutrality and effect solution. The Pharmacopœia requires it to contain an amount of iron and ammonium tartrate corresponding to not less than 13 per cent. of metallic iron.

Iron and Potassium Tartrate.—This compound may be made by a process similar to that given for the preceding scale salt, except that acid potassium tartrate is used in place of acid ammonium tartrate. The hot solution of iron and potassium tartrate is not at once concentrated and spread on glass, but filtered and set aside for twenty-four hours to cool; during this time a precipitate separates and the liquid becomes acid. Upon carefully neutralizing with ammonia water a perfect solution is again produced, which is then concentrated and scaled.

Iron and potassium tartrate is recognized in the British Pharmacopœia under the name Ferrum Tartaratum, and is so prescribed in Great Britain. It occasionally happens that, as in the case of the preceding salt, it has become acid and difficultly soluble, probably owing to careless preservation; in such a case a few drops of ammonia water carefully added to the residue will restore perfect solubility.

The theoretical composition of the salt when anhydrous is $K(FeO)C_4H_4O_6$ or $(CHOH)_2COOKCOO(FeO)$, based upon the equation $Fe(OH)_3 + KHC_4H_4O_6 = K(FeO)C_4H_4O_6 + 2H_2O$. Like all the other scale salts of iron, it contains variable proportions of water. The Pharmacopœia requires the presence of an amount of iron in combination corresponding to 15 per cent. of metallic iron.

Iron and Quinine Citrate.—The official scale compound of this name is unfamiliar to many pharmacists who have been in the habit of handling only the so-called soluble variety. It is prepared by dissolving 12 Gm. of dry quinine (pure alkaloid) in a strong solution of 85 Gm. of ferric citrate, with the aid of 3 Gm. of citric acid, concentrating the solution on a water-bath to a syrupy consistence, and finally scaling the same on plates of glass. The yield is intended to be 100 Gm.

The official iron and quinine citrate is intended chiefly to be used in the form of pills, tablets, etc., but not in solution; for, although it is completely soluble in water, it dissolves very slowly. It is of a reddish-brown color, somewhat resembling ferric citrate in appearance, and deliquesces slowly in damp air.

The Pharmacopœia demands that the scale salt shall contain not less than 11.5 per cent. of dried quinine and an amount of iron corresponding to 13.5 per cent. of that metal. Both can be determined in one sample, the quinine gravimetrically and the iron by the iodometric method, and thus much time and labor saved. The official estimation of the quinine is easily accomplished; the addition of ammonia water to a solution of the salt precipitates the quinine as alkaloid, which, dissolving readily in the chloroform, can be withdrawn and the treatment with chloroform repeated twice, so as to insure the complete removal of the alkaloid. A globular separator (see Fig. 142, page 158) is better adapted for the operation than one of cylindrical shape, as by simple rotation the two liquids are brought into sufficiently intimate contact for abstraction of the alkaloid by the chloroform, and separation takes place rapidly; if shaking must be resorted to, it frequently happens that an emulsion results, which requires considerable time for separation. Owing to the low boiling-point of chloroform (60° C. (140° F.)), the liquid should be evaporated with moderate heat only, so as to avoid loss by spurting, the residue being afterward dried at 100° C. (212° F.) to constant weight.

The residuary aqueous liquid retains all the ferric citrate, and, if 25 Cc. of the same be used, after removal of all the chloroform and ammonia and dilution to 50 Cc., this will represent exactly one-half of the scale salt originally used, and therefore 13.5 Cc. of $\frac{N}{10}$ sodium thiosulphate solution will be necessary to indicate 13.5 per cent. of metallic iron, 1.11 Gm. having been used in the test. One-half of 1.11 is 0.555, and 13.5 per cent. of 0.555 is 0.074925; hence, as each Cc. of the thiosulphate solution represents 0.00555 Gm. of metallic iron, 13.5 Cc. will correspond to 0.074925 Gm., for 0.074925 ÷ 0.00555 = 13.5.

Soluble Iron and Quinine Citrate.—As stated before, this is the salt generally dispensed by pharmacists, and is, in fact, the article usually sold by the jobber when citrate of iron and quinine is ordered. The Pharmacopœia has added the adjective "soluble" to the title of this salt, to distinguish it from the less soluble reddish-brown variety; when the latter is wanted, pharmacists should always specify it by adding the letters U. S. P. to the name.

Soluble iron and quinine citrate differs in composition from the preceding salt only in containing ammonia, which is combined with citric acid, whereby the solubility of the compound is greatly increased, as in the case of iron and ammonium citrate. The ammonia water is added to the solution of iron and quinine citrate first prepared as long as the precipitate formed is redissolved; an excess of ammonia must be carefully avoided. The solution acquires a greenish-yellow color and yields greenish, golden-yellow scales, which readily absorb moisture upon exposure to the air and are rapidly soluble in cold water.

The estimation of the iron and quinine is made exactly as in the plain iron and quinine citrate, the required proportion of each being identical in both salts.

Iron and Strychnine Citrate.—For the preparation of this compound iron and ammonium citrate is generally employed, in order to obtain at once a readily soluble product; 1 Gm. each of strychnine and citric acid are dissolved in about 20 Cc. of water and added to a solution of 98 Gm. of iron and ammonium citrate in its own weight of water, the mixed liquids being concentrated and scaled on glass like other scale salts.

The Pharmacopœia requires for this preparation the presence of not less than 0.9 nor more than 1 per cent. of strychnine and a proportion of ferric citrate corresponding to 16 per cent. of metallic iron. The assay is made in the same manner as prescribed for iron and quinine citrate.

Solution of Ferric Chloride.—An aqueous solution of ferric chloride, $FeCl_3$, containing not less than 29 per cent. of the anhydrous salt. The official directions for preparing this solution consist in treating bright iron wire with hydrochloric acid diluted with about one-half its weight of water, oxidizing the resulting solution by means of nitric and hydrochloric acids, and finally, after addition of a little more hydrochloric acid, bringing the liquid to a definite weight by addition of distilled water.

The mixture of iron, hydrochloric acid, and water is heated on a water-bath for not less than 1¼ hours or until effervescence ceases, which latter is due to the escape of hydrogen, the ferrous chloride formed dissolving in the water, as illustrated by the equation $Fe_2 + 4HCl = 2FeCl_2 + H_4$. Not all the iron is dissolved, an excess being purposely used to facilitate the reaction. The mixture is then boiled and filtered through paper, the flask and wire being rinsed with hot water. A further addition of hydrochloric acid is at once made to the filtrate, to avoid the formation and deposit of ferric oxychloride, as the ferrous chloride is readily oxidized by the air.

The liquid, which has now assumed a deep green color, is poured slowly into a porcelain dish containing nitric acid, and then warmed. A change in color to reddish-brown at once occurs, owing to the conversion of the ferrous into ferric chloride, accompanied by effervescence and escape of red fumes, which may be illustrated by the following equation: $3FeCl_2 + 3HCl + HNO_3 = 3FeCl_3 + NO + 2H_2O$. The red fumes are due to nitrogen tetroxide, NO_2 or N_2O_4, resulting from a union of nitric oxide, NO, with some of the oxygen of the air.

It frequently happens that the color of the liquid remains blackish for some time; this is due either to a union of ferrous chloride with nitric oxide, in which case it disappears upon further heating as oxidation progresses, or, it may be, to an insufficiency of nitric acid and consequent imperfect oxidation.

To remove all nitrogen compounds, the liquid is heated on a sand-bath until free from nitrous odor, after which it is tested for ferrous salt, as prescribed; and if more nitric acid is necessary, this should be added drop by drop to the hot liquid and only as long as effervescence results, as an excess of nitric acid is not readily removed. If ferrous salt is found absent, a test for nitric acid should be made, and, if present, the liquid must be boiled on a sand-bath until entirely free therefrom; this is preferably done with careful addition of small quantities of hydrochloric acid, which facilitates the expulsion of nitric acid by decomposing it, and prevents the formation of oxychloride. Should the liquid, upon boiling to free it from nitric acid, separate a blackish-brown deposit on the sides or bottom of the dish, this would indicate ferric oxychloride, which can only be overcome by careful addition of hydrochloric acid to the hot liquor until a 0.5 per cent. solution of the latter in water remains clear upon boiling and cooling.

The final addition of hydrochloric acid to the liquid is for the purpose of preventing the formation of ferric oxychloride by having an excess of the acid present.

Solution of ferric chloride contains a small amount of free hydrochloric acid, but should be absolutely free from ferrous salt and ferric oxychloride, as well as nitric acid and other nitrogen compounds. Commercial solutions of ferric chloride are frequently contaminated with ferric oxychloride, and nitrous odors are often perceptible.

The official solution has a specific gravity of about 1.315 at 25° C. (77° F.)., and contains nearly 0.382 Gm. of anhydrous ferric chloride in each Cc., or about 175 grains in each fluidounce; its chief use in pharmacy is for the preparation of the tincture of ferric chloride. The Pharmacopœia requires that the solution shall contain an amount of ferric chloride corresponding to 10 per cent. of metallic iron, which is determined volumetrically by the iodometric method, as already explained under Ferric Chloride. 1.11 Gm. of the solution being used for the official test, each Cc. of $\frac{N}{10}$ sodium thiosulphate solution required to discharge the color caused by the liberated iodine represents 0.00555 Gm. of metallic iron, and hence corresponds to ½ per cent. of the 1.11 Gm. taken; 20 Cc. will therefore be required to indicate 10 per cent.

Solution of Ferric Subsulphate.—An aqueous solution of basic ferric sulphate of variable composition. It is prepared by adding 675 Gm. of crystallized ferrous sulphate to a heated mixture of 65 Gm. of sulphuric and 70 Gm. of nitric acid, and 500 Cc. of water; when effervescence ceases the liquid is tested for ferrous salt, and, if this be found present, nitric acid is added drop by drop to the hot liquid as long as it causes effervescence and the disengagement of red fumes. Finally the liquid is boiled until a clear ruby-red solution is obtained entirely free from nitrous odor, and is diluted with water to the weight of 1000 Gm.

The ferrous sulphate is used in the form of a coarse powder, and added to the hot acid mixture in divided portions, in order to avoid a violent reaction. In the presence of nitric and sulphuric acids oxidation takes place, converting the ferrous into a ferric salt, but, owing to an insufficient amount of sulphuric acid, a basic, instead of a normal, ferric sulphate is produced, the composition of which is variable; hence no definite formula can be assigned to it, although the following, $Fe_4O(SO_4)_5$, is used by some to illustrate the nature of the salt. In the preparation of this, as well as the next following solution, copious red vapors are evolved, due to the escape of nitric oxide in the air, and the liquid assumes a black tint temporarily, on account of a union between the ferrous sulphate and nitric oxide; these phenomena have been explained in connection with the manufacture of solution of ferric chloride (p. 561).

If a little sulphuric acid be added to solution of ferric subsulphate, the color becomes lighter, and, if added to the extent of one-half the volume of the latter, a white mass, consisting of anhydrous ferric sulphate, will separate.

The name Monsel's Solution is usually applied to this preparation, which is also prescribed by physicians as solution of persulphate of iron; although chemically incorrect, this last name is sometimes employed in this country when the official solution of the subsulphate is intended, particularly by some of the older physicians.

Solution of ferric subsulphate is a dense solution, having a specific gravity of about 1.548 at 25° C. (77° F.), and is apt to separate a semisolid crystalline whitish mass upon standing, particularly in the cold. This is not a sign of deterioration, but is due to the concentration of the solution, and can be overcome by placing the bottle in warm water for a while and agitating, when perfect solution will be restored. The Pharmacopœia demands that the amount of basic ferric sulphate present in this solution shall correspond to 13.57 per cent. of metallic iron, to be estimated in the same manner as indicated for the other iron solutions.

Solution of Ferric Sulphate.—An aqueous solution of normal ferric sulphate, $Fe_2(SO_4)_3$, containing about 36 per cent. of the salt. This solution is not used medicinally, being employed only for the preparation of other iron compounds. It is made in the same manner as solution of ferric subsulphate, except that a larger proportion of acids is used, a different product being, therefore, obtained. The following equation, $6(FeSO_4 + 7H_2O) + 3H_2SO_4 + 2HNO_3 = 3Fe_2(SO_4)_3 + 2NO + 46H_2O$, shows that the reaction results in the formation of a normal salt, which is the only point of difference in the composition of this and the preceding solution.

Solution of ferric sulphate is known in the British Pharmacopœia as Solution of Persulphate of Iron, but the official Latin title of the United States Pharmacopœia, Liquor Ferri Tersulphatis, is preferable, as at once indicating the true nature of the chemical compound present. It can readily be distinguished from Monsel's Solution by a lower density and lighter color, and also by not separating white ferric sulphate upon addition of one-half its volume of sulphuric acid. The solution has a specific gravity of about 1.432 at 25° C. (77° F.), and is required to contain an amount of ferric sulphate corresponding to not less than 10 per cent. of metallic iron.

Solution of Iron and Ammonium Acetate.—This well-known preparation is usually prescribed by physicians as "Basham's Mixture," or under its old official (Pharmacopœia, 1880) title, Mistura Ferri et Ammonii Acetatis. It is readily prepared by adding to 500 Cc. of solution of ammonium acetate successively 60 Cc. of diluted acetic acid, 40 Cc. of tincture of ferric chloride, 120 Cc. of aromatic elixir, 120 Cc. of glycerin, and sufficient water to bring the total volume up to 1000 Cc.

As its name indicates, the solution contains both iron and ammonium acetates, the former salt, to which the deep-red color of the liquid is due, being formed, at the time of preparation, by mutual decomposition between the ferric chloride and a part of the ammonium acetate; a small amount of ammonium chloride also is formed. It is important that the solution of ammonium acetate be not alkaline, so that, upon addition of the diluted acetic acid, an excess of the latter shall be present, to avoid the formation of basic ferric acetate when the tincture of ferric chloride is added.

Although the Pharmacopœia directs that this preparation should be freshly made when wanted, this is not necessary, as, when prepared strictly according to the present official formula, it keeps well for months, without showing signs of change even in diffused light or during summer weather. The present preparation is twice as strong as that formerly official and contains in each Cc. about 0.00766 Gm. of ferric acetate, or about ½ grain in ½ fluidounce, the average adult dose.

Tincture of Ferric Chloride.—This is a hydro-alcoholic solution of ferric chloride, containing 13.28 per cent. of the anhydrous salt. The Pharmacopœia directs that 350 Cc. of solution of ferric chloride shall be mixed with sufficient alcohol to yield 1000 Cc.; this will require slightly more than 650 Cc. of alcohol, on account of the contraction of volume which invariably results when aqueous liquids and alcohol are mixed. The official directions, to set the mixture aside for a period of three months, are for the purpose of allowing certain changes to take place before dispensing the tincture; these changes are due to reaction between the acid solution of ferric chloride and alcohol, resulting in the formation of ethyl chloride and other ethereal products, which modify the odor of the preparation to some extent, and are said also to possess marked medicinal properties. By some authorities it is claimed that these changes will not be completed at the end of three months, and that, in fact, they will continue for a period of six or nine months.

Occasionally the mixture is found to deposit a yellowish-brown sediment; this is due to ferric oxychloride present in the solution of ferric chloride used, and is an evidence that the latter preparation was not properly made.

Tincture of ferric chloride contains, in each Cc., about 0.1334 Gm. of anhydrous ferric chloride, equivalent to about 60 grains in each fluidounce. Upon exposure to sunlight it is gradually changed in color, assuming a greenish-brown tint, owing to reduction of the ferric to ferrous salt; hence it should be protected from strong light.

The proportion of ferric chloride present in the official tincture corresponds to 4.58 per cent. of metallic iron, and is determined in the usual manner with potassium iodide and sodium thiosulphate. In order to insure the absence of ferrous salt and other impurities in the official test, the Pharmacopœia directs that 2.22 Gm. of the tincture be evaporated to dryness, mixed with 2 Cc. each of hydrochloric acid and solution of hydrogen dioxide and again evaporated to dryness before it is dissolved in water, and further treated with hydrochloric acid and potassium iodide. Each Cc. of the sodium thiosulphate solution used corresponds to 0.00555 Gm. of metallic iron, which is equivalent to ¼ per cent. of 2.22 Gm., and not less than 18.3 Cc. will therefore be required to indicate 4.58 per cent. of 2.22 Gm. or 0.101676 Gm., for $0.101676 \div 0.00555 = 18.32$.

Besides the official preparations of iron, the following are employed:

Albuminate of Iron.—This compound occurs in the form of yellowish-brown scales, obtained by concentrating an alkaline solution of ferric albuminate (see Solution of Albuminate of Iron) with the aid of a low heat, spreading the same on plates of glass and drying at a moderate temperature. It represents between 3 and 4 per cent. of metallic iron, and must be carefully preserved.

Arsenate of Iron.—This preparation, as found in the market, is of a variable composition, and consists chiefly of ferrous arsenate, $Fe_3(AsO_4)_2.6H_2O$, with ferric arsenate and some iron oxide. It is recognized in the British Pharmacopœia as iron arsenate, and directed to be made by mixing a solution of sodium arsenate with one of ferrous sulphate and adding some sodium bicarbonate. Ferrous arsenate is precipitated, which is well washed and dried, in the meantime undergoing oxidation and changing from greenish white to olive green or bluish green in color.

Benzoate of Iron. Ferric Benzoate. $Fe(C_7H_5O_2)_3$ or $(C_6H_5\text{-}COO)_3Fe$.—This salt may be obtained as a pale-brownish powder by adding a concentrated solution of sodium benzoate to a solution of ferric sulphate, washing the resulting precipitate with a little cold water, and drying the same.

Bromide of Iron. Ferrous Bromide. $FeBr_2$.—This compound is prepared by direct union of iron and bromine in the presence of water; an excess of iron wire is used, and when a pale-green solution results it is filtered and evaporated to dryness in a bright iron dish. It forms a dark, almost black mass, which turns brown through oxidation upon exposure to air; hence it must be preserved in tightly stoppered bottles.

Dialyzed Iron.—Under this name a solution of a highly basic ferric oxychloride has been used by physicians for many years. It is recognized in the German Pharmacopœia by the names *liquor ferri oxydati dialysati* and *liquor ferri oxychlorati*. The official German preparation is not obtained by dialysis, but simply by dissolving freshly prepared ferric hydroxide in water, with the aid of a very small quantity of hydrochloric acid and a gentle heat. The process usually followed in this country consists in saturating a solution of ferric chloride with freshly made ferric hydroxide, the liquid being placed in a dialyzer (see page 166) and suspended in water, which is frequently renewed as long as the latter shows any reaction for chlorides. Complete removal of ferric chloride is neither practicable nor desirable, and highly basic oxychlorides give no reaction with silver nitrate. The solution of ferric oxychloride remaining in the dialyzer is then diluted with sufficient water so that 100 parts by weight, when evaporated and dried at a temperature not above 100° C. (212° F.), shall yield 5 parts of solid residue. The composition of the ferric oxychloride found in commercial dialyzed iron varies, ranging between $FeCl_3 + 10F_2O_3$, and $FeCl_3 + 35Fe_2O_3$; still more highly basic oxychlorides can be obtained by dialysis, but the solutions are apt to gelatinize on standing.

Ferrocyanide of Iron. Ferric Ferrocyanide. $Fe_4(Fe(CN)_6)_3$.—When a solution of potassium ferrocyanide is gradually added to a dilute solution of ferric sulphate a dark-blue precipitate having the above composition is obtained. The precipitate must be well washed with boiling water, to remove all potassium sulphate, and is then dried.

Glycerophosphate of Iron. Ferric Glycerophosphate. $Fe_2(C_3H_5(OH)_2PO_4)_3$.—This salt may be obtained by dissolving freshly precipitated and well-washed ferric hydroxide in an aqueous solution of glycerophosphoric acid, evaporating the solution in a vacuum apparatus to a syrupy consistence, and then spreading on plates of glass and drying at a gentle heat. It forms yellow scales, soluble in water and diluted alcohol.

Iodide of Iron. Ferrous Iodide. FeI_2.—This preparation is obtained by first making a solution of ferrous iodide, in a manner similiar to that followed for bromide of iron, and evaporating this to dryness in a bright iron dish. It occurs as a very deliquescent black mass, which must be carefully preserved in a tightly stoppered bottle.

Lactate of Iron. Ferrous Lactate. $Fe(C_3H_5O_3)_2 + 3H_2O$ or $(CH_3CHOHCOO)_2Fe + 3H_2O$.—This salt may be prepared by double decomposition between solutions of calcium lactate and ferrous sulphate, the newly formed calcium sulphate being completely removed by addition of alcohol; the filtrate is finally evaporated and crystallized. It may also be obtained by digesting pure iron wire with diluted lactic acid until reaction ceases, then filtering, concentrating, and crystallizing the solution. In the first process the reaction is as follows: $Ca(C_3H_5O_3)_2.5H_2O + FeSO_4.7H_2O = Fe(C_3H_5O_3)_2 + CaSO_4 + 12H_2O$; while in the second process ferrous lactate is formed with elimination of hydrogen; thus, $Fe_2 + 4HC_3H_5O_3 = 2Fe(C_3H_5O_3)_2 + H_4$.

Two varieties of ferrous lactate occur in commerce, one in well-defined crystalline crusts and another in the form of a crystalline powder. The first-named is to be preferred for pharmaceutical purposes; it is, as a rule, more soluble and less likely to have become oxidized. Ferrous lactate should be preserved in tightly stoppered bottles, in a dry place, as upon exposure to moist air it is gradually converted into a ferric salt.

Malate of Iron.—Impure ferrous malate occurs in the form of a blackish-green mass, obtained by digesting the juice of sour apples with iron filings, filtering, and evaporating the solution to the consistence of an extract. It is recognized in the German Pharmacopœia under the name of Extractum Ferri Pomatum.

Oxalate of Iron. Ferrous Oxalate. FeC_2O_4 or $(COO)_2Fe$.—This salt may be conveniently prepared by mixing a solution of acid ammonium oxalate with one of ferrous sulphate; the lemon-yellow precipitate of ferrous oxalate is well washed with water until a reaction for sulphuric acid is no longer obtained, and then dried. This process affords a better yield than if ferrous sulphate be treated with pure oxalic acid, since some of the salt would be lost by solution in the diluted sulphuric acid.

Phosphate of Iron.—This compound has been mentioned in connection with the soluble salt of the same name. It is a variable mixture of ferrous and ferric phosphates with ferric oxide, and is recognized in the British Pharmacopœia, which directs it to be prepared by adding a solution of sodium phosphate to one of ferrous sulphate, finally adding some sodium bicarbonate. The precipitate of ferrous phosphate, $Fe_3(PO_4)_2$, is washed and dried, during which time it is slowly oxidized. Phosphate of iron is a slate-blue amorphous powder, insoluble in water.

Peptonate of Iron.—If egg-albumen be digested with pepsin and very dilute hydrochloric acid for some time at a temperature not exceeding 40° C. (104° F.), a solution of peptone will be obtained, which, after being neutralized with solution of soda and added to a solution of ferric oxychloride, yields a precipitate of ferric peptonate. In order to obtain the compound in soluble form the precipitate is dissolved in water with the aid of a little hydrochloric acid and heat, the solution evaporated to a syrupy consistence, and spread on plates of glass, to be dried at a temperature not above 30° C. (86° F.).

Saccharated Oxide of Iron.—This preparation, known also as soluble oxide of iron, is officially recognized in the German Pharmacopœia, and is used to some extent in this country. It is obtained by adding to freshly prepared ferric hydroxide a given proportion of sodium hydroxide solution and sugar, heating the mixture to perfect solution, then evaporating to dryness, powdering, and incorporating with it sufficient sugar to bring the product up to a definite weight, representing the equivalent of 3 per cent. of metallic iron. The exact composition of the reddish-brown powder is as yet not clearly understood; it is considered to be a sodio-ferric saccharate, the presence of the alkali being essential, as, with sugar alone, ferric hydroxide does not form a perfectly soluble compound.

Salicylate of Iron. Ferrous Salicylate. $Fe(C_7H_5O_3)_2$ or $(C_6H_4(OH)COO)_2Fe$.—This is best prepared by dissolving freshly precipitated ferrous carbonate in water by means of salicylic acid, with the aid of gentle heat, filtering, and evaporating the solution to dryness on a water-bath.

Valerate of Iron. Ferric Valerate.—This salt, formerly officially recognized as ferric valerianate, is best obtained by double decomposition between cold solutions of ferric sulphate and sodium valerate, washing the resulting precipitate with a little cold water, and drying at a moderate temperature. The composition of ferric valerate is variable, depending upon the care employed in washing the precipitate and the temperature at which it is dried. The normal salt would have the composition $Fe(C_5H_9O_2)_3$, but the commercial product is mixed often with basic salt, as shown by its increased yield of ferric oxide upon ignition.

Ferric valerate is rarely used in other than pill-form, although it is readily soluble in alcohol.

Solution of Albuminate of Iron.—An aromatic, alkaline solution of ferric albuminate prepared, according to the German Pharmacopœia, as follows: a solution of 35 parts of dry egg-albumen in 1000 parts of water is slowly added to a mixture of 120 parts of solution of oxychloride of iron and 1000 parts of water; the resulting precipitate is well washed with water until all chlorine has been removed, and then dissolved in 3 parts of solution of soda (sp. grav. 1.17) diluted with 50 parts of water. To this solution are added 150 parts of alcohol, 100 parts of cinnamon water, 2 parts of aromatic tincture, and sufficient water to bring the total weight up to 1000 parts. It represents about 0.4 per cent. of metallic iron.

Subcarbonate of Iron.—Under this name an amorphous reddish-brown powder has long been known in pharmacy, and was at one time recognized in the Pharmacopœia (1870). It is a variable mixture, the composition depending upon age and the temperature at which it has been dried, and consists chiefly of ferric oxide and hydroxide with some ferrous carbonate. The manner of preparing it is to mix solutions of ferrous sulphate and sodium carbonate together, whereby greenish-white ferrous carbonate is precipitated; this is thoroughly washed with water and dried, during which operation it rapidly darkens and becomes oxidized, with the elimination of carbon dioxide. Subcarbonate of iron is practically identical with ferric oxyhydrate, $Fe_2O_3 + Fe_2(OH)_6$, and is often designated as red steel-dust by the public.

Syrup of Arsenate of Iron.—A preparation of the *National Formulary* containing about $\frac{1}{60}$ grain of ferric arsenate, Fe_2AsO_4, in each fluidrachm. It is made by preparing a solution of ferric arsenate from sodium arsenate and ferric citrate, and mixing this with simple syrup, the ferric arsenate being held in solution by the newly formed sodium citrate.

Syrup of Citro-iodide of Iron.—This preparation, also known as "tasteless syrup of iodide of iron," is made, according to the *National Formulary*, by dissolving iodine in a solution of ferrous iodide and adding this solution to a solution of potassium citrate; as soon as a deep-green color has developed sugar is added and dissolved by agitation. Each fluidounce contains about 29 grains of ferric iodide, FeI_3, equivalent to about 0.0635 Gm. in each Cc.

Syrup of Soluble Oxide of Iron.—This syrup may be conveniently prepared extemporaneously as wanted, by forming a solution of equal parts by weight of saccharated oxide of iron, water, and simple syrup. This is the formula given by the German Pharmacopœia; a more tedious process for making the syrup from solution of ferric chloride is given in the *National Formulary*. Each fluidounce of the syrup represents about 6½ grains of metallic iron, or about 0.0143 Gm. in each Cc.

Tincture of Citro-chloride of Iron.—The *National Formulary* directs this preparation, which is better known as "tasteless tincture of iron," to be made by adding sodium citrate to a diluted solution of ferric chloride and heating until perfect solution is effected. Alcohol is then added, and finally sufficient water to make up the required volume. The tincture is of a deep-green color, and the amount of iron represented is about the same as in the official tincture of ferric chloride.

CHAPTER XLIX.

THE COMPOUNDS OF MANGANESE AND CHROMIUM.

Of these two metals the Pharmacopœia recognizes but 4 compounds, and even these are not frequently employed. The official preparations are as follows:

Official English Name.	Official Latin Name.
Precipitated Manganese Dioxide,	Mangani Dioxidum Præcipitatum.
Manganese Hypophosphite,	Mangani Hypophosphis.
Manganese Sulphate,	Mangani Sulphas.
Chromium Trioxide,	Chromii Trioxidum.

Precipitated Manganese Dioxide.—This compound consists chiefly of manganese dioxide with small amounts of other oxides of manganese. Being obtained by precipitation, it is free from foreign matter and therefore well suited for internal use. The official directions for its preparation involve the precipitation of manganous hydroxide from a solution of the sulphate by addition of ammonia water, and its conversion into manganic hydroxide by means of hydrogen dioxide, which is then dried at 150° C. (302° F.) and changed to manganese dioxide, the water of hydration being nearly all driven off at that temperature. The following equations indicate the successive steps in the manufacture: $MnSO_4 + 2NH_4OH = Mn(OH)_2 + (NH_4)_2SO_4$; $Mn(OH)_2 + H_2O_2 = Mn(OH)_4$ or $MnO_2 + 2H_2O$. It is a very fine black powder, which, when heated to redness, gives off oxygen and is converted into manganoso-manganic oxide Mn_3O_4.

The Pharmacopœia requires that precipitated manganese dioxide shall contain not less than 80 per cent. of pure MnO_2, but some manufacturers are offering an article of over 90 per cent. purity. The determination is made volumetrically with oxalic acid. In the official test $\frac{N}{10}$ oxalic acid solution is added in excess, 50 Cc. to 0.2 Gm. of the sample, and heated in the presence of sulphuric acid, after which the excess of oxalic acid is titrated with $\frac{N}{10}$ potassium permanganate solution. The equation $MnO_2 + (H_2C_2O_4\text{-}+2H_2O) + H_2SO_4 = 2CO_2 + MnSO_4 + 4H_2O$ shows that 1 molecule or 86.36 Gm. of manganese dioxide is capable of oxidizing 1 molecule or 125.10 Gm. of crystallized oxalic acid, and each Cc. of $\frac{N}{10}$ oxalic acid solution, containing 0.006255 Gm. of the acid, will therefore require 0.004318 Gm. of pure manganese dioxide. As the Pharmacopœia demands that not more than 13 (12.95) Cc. of the potassium permanganate solution shall be necessary to produce a slight pink tint, it requires that 37 (50–13) Cc. of the oxalic acid solution shall be oxidized by the 0.2 Gm. of precipitated manganese dioxide used, which would indicate not less than 80 per cent. purity, for $0.004318 \times 37 = 0.159766$, and 0.159766 is 79.88 + (practically 80) per cent. of 0.2.

Commercial native manganese dioxide, also known as black oxide of manganese, or pyrolusite, is no longer recognized officially. It is found in different parts of Russia, Germany, France, Spain, and Great Britain, and also in Nova Scotia, Vermont, Pennsylvania, and other parts of North America. Sometimes it is found nearly pure, but is generally associated with other manganic ores, particularly with the inferior brown manganite, and often with iron, lime, baryta, silica, etc. Pyrolusite is the most important and most abundant manganese mineral. When pure it consists of 63.19 per cent. of manganese and 36.81 per cent. of oxygen. The only use to which black oxide of manganese is put in pharmacy is in the preparation of pure chlorine water, and for this purpose it should contain at least 65–70 per cent. of manganese dioxide.

Manganese Hypophosphite. $Mn(PH_2O_2)_2 + H_2O$.—This salt may be made by decomposing a solution of calcium hypophosphite with one of manganous sulphate, stirring the mixture well, and setting aside in a warm place to allow the calcium sulphate to separate, after which the solution is filtered and allowed to crystallize. The Pharmacopœia requires that the salt shall contain not less than 97 per cent. of pure $Mn\,(PH_2O)_2$, which may be determined as in the case of other hypophosphites. The absence of calcium is demanded, as also of carbonate and phosphate.

Manganese Sulphate. Manganous Sulphate. $MnSO_4 + 4H_2O$.—This salt is obtained by heating a mixture of manganese dioxide and sulphuric acid to dull redness, in a crucible, for some time; when cool, the mass is treated with water and filtered. The solution, if iron be present, is digested with manganous carbonate, filtered, concentrated and crystallized at a temperature not below 20° C. (68° F.). If the solution be allowed to crystallize at a temperature approaching 5° C. (41° F.), a salt will be obtained containing 7 molecules, or nearly 46 per cent., of water, while the official salt should contain only 4 molecules, or 32.29 per cent.

Manganous sulphate is used for the preparation of other manganese salts by mutual decomposition, such as the carbonate, hypophosphite, and iodide, which are occasionally used in pharmacy.

Chromium Trioxide. Chromic Anhydride. CrO_3.—This compound, formerly recognized in the Pharmacopœia as chromic acid, and still commercially better known by that name, may be obtained by allowing strong sulphuric acid to act on a cold saturated solution of potassium dichromate, chromium trioxide being set free, as shown by the following equation: $K_2Cr_2O_7 + 2H_2SO_4 = 2CrO_3 + 2KHSO_4 + H_2O$: this is due to the fact that chromic acid proper, H_2CrO_4, like arsenous and carbonic acids, can exist only in solution, and upon evaporation of the latter is at once converted into its anhydride. The mixture becomes heated, and upon cooling separates needle-shaped crystals, which are drained and dried upon porous tiles. When prepared by the ordinary methods chromium trioxide is usually contaminated with sulphuric acid and potassium salts, the former rendering it very hygroscopic. Inasmuch as the Pharmacopœia demands the absence of sulphuric acid, the process of manufacture is probably modified by washing the crystals dried on porous plates with small quantities of strong nitric acid, again drying on plates, and finally heating to 60–80° C. (140–176° F.) in order to remove adhering nitric acid. The color of commercial chromium trioxide is not uniform, depending upon the purity of the article; if pure, the proper color is dark purplish-red, while a light scarlet-red color usually indicates the presence of sulphuric acid.

The Pharmacopœia requires that the official chromium trioxide shall contain not less than 90 per cent. of pure CrO_3, to be determined by the iodometric method by adding to a solution of 0.083 Gm. of the compound 2 Cc. of hydrochloric acid and 1 Gm. of potassium iodide, and then titrating the liberated iodine with $\frac{N}{10}$ sodium thiosulphate solution, using starch test-solution as an indicator. The operation is considered completed when the deep blue color of iodized starch has been changed to a light green. The reactions involved in this test may be illustrated by the following equations, the first step being the conversion of chromium trioxide into chromic acid by solution of the former in water: $CrO_3 + H_2O = H_2CrO_4$; $2H_2CrO_4 + 6HCl = 2CrCl_3 + O_3 + 5H_2O$; $6KI + 6HCl = 6KCl + 6HI$; $6HI + O_3 = I_6 + 3H_2O$; showing that for every molecule or 99.34 Gm. of pure CrO_3 present 3 atoms or 377.7 Gm. of iodine will be liberated; hence each Cc. of the sodium thiosulphate solution, corresponding to 0.01259 Gm. of iodine, will also correspond to 0.003311 Gm. of CrO_3, which is equal to 4 per cent. of the 0.083 Gm. of the sample taken for the test. If 1 Cc. of the sodium thiosulphate solution corresponds to 4 per cent., it will require 22.5 Cc. to indicate 90 per cent. purity, as stated in the Pharmacopœia.

Owing to its ready decomposition by organic substances, often with explosive violence, chromic anhydride should never be brought into contact with alcohol or glycerin, and should always be weighed on watch-glasses, never on paper; if its aqueous solution requires filtration this must be done by means of asbestos or glass-wool.

CHAPTER L.

THE COMPOUNDS OF MERCURY.

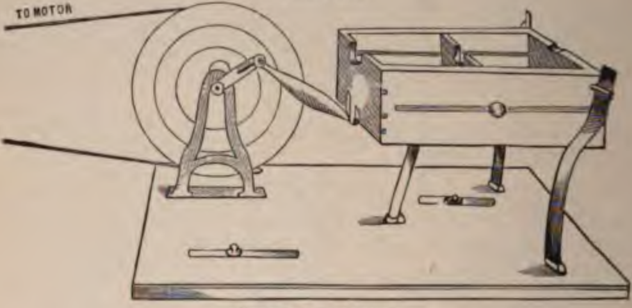
NEXT to the preparations of iron, those of mercury are the most important obtained from the heavy metals. Like the iron compounds, they are divided into two series, designated as mercurous and mercuric compounds, respectively. In mercurous compounds, mercury appears univalent, while in mercuric compounds it acts like a bivalent element. The Pharmacopœia recognizes metallic mercury and 17 preparations of it and its compounds, as shown by the following list:

Official English Name.	Official Latin Name.
Mercury,	Hydrargyrum.
Mercury with Chalk,	Hydrargyrum cum Creta.
Ammoniated Mercury,	Hydrargyrum Ammoniatum.
Mild Mercurous Chloride,	Hydrargyri Chloridum Mite.
Yellow Mercurous Iodide,	Hydrargyri Iodidum Flavum.
Corrosive Mercuric Chloride,	Hydrargyri Chloridum Corrosivum.
Red Mercuric Iodide,	Hydrargyri Iodidum Rubrum.
Yellow Mercuric Oxide,	Hydrargyri Oxidum Flavum.
Red Mercuric Oxide,	Hydrargyri Oxidum Rubrum.
Mass of Mercury,	Massa Hydrargyri.
Mercurial Ointment,	Unguentum Hydrargyri.
Mercurial Plaster,	Emplastrum Hydrargyri.
Ointment of Ammoniated Mercury,	Unguentum Hydrargyri Ammoniati.
Ointment of Mercuric Nitrate,	Unguentum Hydrargyri Nitratis.
Ointment of Yellow Mercuric Oxide,	Unguentum Hydrargyri Oxidi Flavi.
Ointment of Red Mercuric Oxide,	Unguentum Hydrargyri Oxidi Rubri.
Mercuric Oleate,	Oleatum Hydrargyri.
Solution of Mercuric Nitrate,	Liquor Hydrargyri Nitratis.

Mercury. Hg.—Nearly all commercial mercury is obtained by roasting the ore known as cinnabar, crude native sulphide of mercury, the sulphur escaping as sulphur dioxide, while metallic mercury is condensed and collected in suitable apparatus. As thus obtained, it is usually contaminated with lead, copper, and other metals, from which it is freed by treatment with diluted nitric acid; it is finally washed with water and dried. On a small scale mercury may readily be purified by shaking with solution of ferric chloride and subsequently washing with water. For medicinal purposes, only pure redistilled mercury, which possesses a bright lustre, should be used; if contaminated with dust or other mechanical impurities, mercury may be successfully strained through a piece of close muslin or chamois skin. For weighing small quantities of mercury, it is most conveniently transferred from the stock bottle to the balance by means of a drop-tube or pipette, as owing to its great cohesiveness it cannot be poured readily from a bottle.

Mercury with Chalk.—Although not so much used as formerly, this preparation, known also as "Gray Powder," is still a very important one, as it represents mercury in a state of fine division in powder-form, and is frequently used in infantile disorders. The official method of preparation depends upon the extinguishment of the mercury by means of succussion, 38 Gm. of mercury being shaken with 10 Gm. of clarified honey, for six hours or longer in a strong bottle; this is best effected in a mechanical shaker, such as is shown in Fig. 295, which can readily be attached to a water-motor connected with a hydrant. The mixture of mercury and honey is afterward added to a thick, creamy paste, made of 57 Gm. of prepared chalk and a sufficient quantity of water, the whole being triturated until a uniform mixture results, which is finally dried at the ordinary temperature, and should be reduced to powder without trituration.

FIG. 295.



Mechanical shaker.

In this state of fine division mercury is very prone to oxidation if exposed to air and light; hence the powder should be kept well protected from both. While traces of mercurous oxide cannot be entirely avoided, the presence of mercuric oxide should carefully be guarded against, and any change in color from gray to pink or reddish, indicating dangerous oxidation, renders the article unfit for use; neither should mercury with chalk be dispensed if the color has turned very dark gray or blackish, as this shows excessive mercurous oxidation. In the official test, mercurous oxide is detected by precipitation, as calomel by hydrochloric acid, while the mercuric oxide is converted into mercuric chloride, and is then precipitated either as mercuric sulphide by hydrogen sulphide, or as calomel (being afterward reduced to metallic mercury) by stannous chloride.

Ammoniated Mercury. NH_2HgCl.—This compound, better known as white precipitate, is prepared by pouring a solution of mercuric chloride slowly, with constant stirring, into ammonia water, when the following reaction occurs: $HgCl_2 + 2NH_4OH = NH_2HgCl + NH_4Cl + 2H_2O$. The Pharmacopœia directs a solution of 100 Gm. of mercuric chloride in 2000 Cc. of distilled water, which, after filtration to remove any calomel present, is added to 150 Cc. of 10 per cent. ammonia water; both liquids are used cold, and the resulting precipitate is washed with 400 Cc. of cold water to which 20 Cc. of ammonia water have been added. Finally, the precipitate is dried in a dark place at a temperature not exceeding 30° C. (86° F.). These specific directions are for the purpose of avoiding the formation of a basic yellow compound, $NH_2(Hg_2O)Cl$, which is likely to occur on exposure to light or heat, and even excessive washing with plain water.

The constitution of ammoniated mercury may be explained in two different ways. The simplest way is to consider it as mercuric chloride in which an atom of chlorine has been replaced by the amido group NH_2, and in that case the name mercuric chloramide will be appropriate; the other view is that the compound is derived from ammonium chloride by replacement of two hydrogen atoms by a bivalent atom of mercury, as suggested by the name mercuric ammonium chloride. The Pharmacopœia requires that it shall contain not less than 78 nor more than 80 per cent. of mercury, and if the process of manufacture has been carefully conducted about 93 Gm. of product will be obtained, which will represent very nearly 74 Gm., or 79 + per cent., of mercury.

Ammoniated mercury is known also as amido-chloride of mercury, and is sometimes prescribed by German physicians as *hydrargyrum amidato-bichloratum.*

Mild Mercurous Chloride. HgCl.—This well-known salt, commonly called calomel, is prepared by subliming a mixture of mercurous sulphate and sodium chloride in proper proportions. In order to obtain the product in the form of a soft, fine powder, the vapors are conducted into a spacious chamber into which steam is introduced simultaneously; the presence of aqueous vapor also frees the sublimate from mercuric chloride, some of which is always formed, by solution in the condensed water. Thus obtained, the product is known as hydrosublimed calomel and is recognized in the German Pharmacopœia as *hydrargyrum chloratum vapore paratum.* When mercurous chloride is sublimed without steam it becomes necessary to reduce the crystalline sublimate to fine powder and wash it thoroughly with water until the washings are no longer affected by ammonia water or ammonium sulphide, showing the complete removal of mercuric chloride.

The mercurous sulphate used in the above process is made by moistening mercuric sulphate with water, adding an equivalent amount of mercury (198.5 parts for 293.85 parts of mercuric sulphate), and triturating the mixture until all globules of mercury disappear. The reaction between mercurous sulphate and sodium chloride when heated together is shown by the following equation: $Hg_2SO_4 + 2NaCl = 2HgCl + Na_2SO_4$.

In France very finely divided calomel, prepared by precipitation, as directed by the Pharmacopœia of that country, is known as *précipité blanc,* which, translated, means white precipitate; care is necessary not to confound this with ammoniated mercury, known in this country as white precipitate, when dispensing French prescriptions.

The appearance of calomel depends largely upon the degree of mechanical division; while usually white, the finer the powder the more yellowish the tint. When exposed to light it gradually undergoes decomposition and assumes a grayish color, mercuric chloride being formed, with the elimination of mercury.

Calomel has sometimes been prescribed by continental physicians under the names "aquila alba" and "mercurius dulcis."

Yellow Mercurous Iodide. HgI.—The official process for the preparation of mercurous iodide involves two distinct steps. First, mercurous nitrate is made by treating 50 Gm. of mercury with a mixture of 20 Cc. each of nitric acid and water, in a dark place, until reaction ceases and a little mercury remains undissolved; the salt separates in the form of crystals having the composition $HgNO_3 + H_2O$, which are drained and dried on paper in the dark. 40 Gm. of the crystallized mercurous nitrate are then dissolved in 650 Cc. of distilled water acidulated with 6 Cc. of nitric acid, and to this solution is added, slowly and with constant stirring, a solution of 16 Gm. of potassium iodide in 32 Cc. of water, when the following reaction occurs: $(HgNO_3 + H_2O) + KI = HgI + KNO_3 + H_2O$. The precipitate is washed with 10 successive portions of 500 Cc. each of distilled water to remove all potassium nitrate and free acid, and lastly dried on paper in the dark, at a temperature not exceeding 40° C. (104° F.).

The addition of nitric acid is made to prevent the formation of a basic compound, which might otherwise occur; it is also important that the potassium iodide be added to the mercurous nitrate, lest, by a reversal of the process, mercuric salt be formed, which enters into solution as potassium mercuric iodide, while mercury is precipitated, a reaction well known to occur between alkali iodides and mercurous iodide, and illustrated by the equation $2HgI + 2KI = (HgI_2 + 2KI) + Hg$.

Mercurous iodide must carefully be protected from light, as it readily undergoes decomposition. The color of the salt when pure is bright yellow; hence all preparations of a green or greenish-yellow color must be looked upon as impure, the latter colors being due to admixture of metallic mercury, which in a finely divided state is blue, and consequently causes a greenish mixture with the pure yellow salt.

Much green iodide of mercury is still sold by manufacturers, having been recognized in the Pharmacopœias of 1870 and 1880, but its production is due to a faulty process of preparation. When mercury and iodine, or mercury and mercuric iodide, are triturated together, yellow mercurous iodide is formed with variable proportions of mercuric iodide, some of the mercury remaining uncombined in a finely divided form; upon subsequent washing with alcohol the mercuric iodide is removed, leaving the insoluble mercurous salt intimately mixed with finely divided mercury, and of a green color. Similar results are likely to occur if mercurous iodide be precipitated from strong neutral solutions of mercurous nitrate by means of potassium iodide; hence the Pharmacopœia directs a dilute acid solution.

Mercurous iodide has been associated with syrup of ferrous iodide in prescriptions, but such mixtures are incompatible, metallic mercury being deposited, a reaction similar to that explained above taking place, and mercuric iodide held in solution by the ferrous iodide.

Corrosive Mercuric Chloride. $HgCl_2$.—This compound, more familiarly known as corrosive sublimate, is obtained by sublimation of an intimate mixture of mercuric sulphate and sodium chloride, both in the form of powder. Mercuric chloride is formed as the result of mutual decomposition; thus, $HgSO_4 + 2NaCl = HgCl_2 + Na_2SO_4$. The heat necessary for the process is likely to decompose some of the mercuric sulphate, with the formation of mercurous chloride, which is volatilized and sublimed along with the mercuric salt. The British Pharmacopœia directs the addition of a small portion of manganese dioxide to the mixture before subliming it, for the purpose of preventing the formation of mercurous salt.

Commercial mercuric chloride occurs in heavy crystalline masses, and is usually contaminated somewhat with calomel; hence perfectly clear solutions can rarely be obtained, even with distilled water. For dispensing purposes only the chemically pure article obtained by recrystallization should be used.

Aqueous solutions of mercuric chloride, if exposed to light, gradually undergo decomposition, liberating hydrochloric acid and depositing calomel. The presence of ammonium chloride, however, prevents the change.

The pharmacopœial test for the presence of arsenic in mercuric chloride depends upon the solubility of arsenic sulphide in ammonia water and its subsequent detection by the Gutzeit test, mercuric sulphide being insoluble in ammonia water.

Red Mercuric Iodide. HgI_2.—This salt is prepared by mutual decomposition between mercuric chloride and potassium iodide, the official directions being to pour a solution of 40 Gm. of the former salt and a solution of 50 Gm. of the latter, simultaneously, into a large volume of water, with active stirring, when the following reaction occurs: $HgCl_2 + 2KI = HgI_2 + 2KCl$. The official formula employs the two salts very nearly in the proportion indicated in the foregoing equation, which are 4 and 4.9+, respectively; an excess of either salt must be avoided, since loss by formation of a soluble compound would result, an excess of potassium iodide producing potassium mercuric iodide ($HgI_2 + 2KI$) and an excess of mercuric chloride causing the formation of mercuric iodochloride ($HgI_2 + 2HgCl_2$ or $Hg_3I_2Cl_4$).

Mercuric iodide is dimorphous, occurring crystallized both in the form of scarlet-red quadratic octahedra and yellow rhombic prisms, but the Pharmacopœia recognizes the salt only in the form of an amorphous scarlet-red powder, which is obtained by the official method of preparation. When exposed to light, mercuric iodide gradually becomes paler in color, and should therefore be preserved in dark bottles. It is soluble in solutions of metallic iodides and sodium thiosulphate, as well as alcohol, olive oil, castor oil, chloroform, glycerin, and glacial acetic acid, forming colorless solutions in each case.

Yellow Mercuric Oxide. HgO.—The official formula for the preparation of this compound directs that a strong solution of 100 Gm. of mercuric chloride be poured slowly, with constant stirring, into a dilute solution of 40 Gm. of 90 per cent. sodium hydroxide; amorphous mercuric oxide is precipitated, while sodium chloride enters into solution. The mixture is allowed to stand at a moderate temperature for an hour, to facilitate complete decomposition, after which the liquid is decanted and the precipitate repeatedly washed until free from alkali, drained, and dried on paper, in a dark place, at a temperature of 30° C. (86° F.).

Mercuric salts do not form hydroxides when added to alkali hydroxides, but mercuric oxide is precipitated instead, as shown by the equation $HgCl_2 + 2NaOH = HgO + 2NaCl + H_2O$. It is important that the alkali be used in excess, otherwise a dark-colored oxychloride will be formed; hence the mercuric chloride solution is poured into the alkali solution in the official process. From the above equation it will be seen that 1 molecule (or 268.86 parts) of mercuric chloride requires 2 molecules (or 79.52 parts) of sodium hydroxide for complete precipitation; hence 100 Gm. $HgCl_2$ will require 29.6 Gm. NaOH; official sodium hydroxide containing 90 per cent. of NaOH, the necessary excess of alkali is assured in the formula of the Pharmacopœia, as 90 per cent. of 40 Gm. is 36 Gm. It is essential that the sodium hydroxide used be free from carbonate, otherwise mercuric carbonate will be formed. Potassium hydroxide may be used in place of sodium hydroxide, but ammonia is inadmissible, owing to the formation of ammoniated mercury. In order to insure a bright orange-yellow product, heat and light must be excluded during precipitation and drying; unless protected from light, the color of the oxide gradually darkens on keeping, and if exposed to direct sunlight decomposition rapidly occurs.

Yellow mercuric oxide, being in a state of very fine division, is more active and more sensitive than the red oxide; it is chemically identical with the latter, but differs from it in the molecular arrangement of its particles, being devoid of all crystalline structure. When digested with a solution of oxalic acid, yellow mercuric oxide forms white mercuric oxalate, while the red oxide remains unaffected.

Red Mercuric Oxide. HgO.—Although the name "red precipitate" is commonly applied to this compound, it is never obtained by precipitation, but always by calcination. As a rule, mercuric nitrate is triturated with metallic mercury until the latter is extinguished; the mixture is then heated in a porcelain dish until yellowish or reddish vapors cease to be evolved and mercuric oxide remains. The metallic mercury is oxidized at the expense of the nitric acid expelled from the mercuric nitrate, and the process may be illustrated by the following equation: $2Hg(NO_3)_2 + Hg_2 = 4HgO + 4NO_2$.

Red mercuric oxide occurs as a crystalline powder or in crystalline scales of an orange-red color, and by trituration with alcohol is gradually converted into a yellowish-red powder. When exposed to light, it darkens in color, but more slowly than the yellow oxide, and, unlike the latter, it is not affected by hot solution of oxalic acid.

Solution of Mercuric Nitrate.—An acid liquid containing about 60 per cent. of mercuric nitrate and about 11 per cent. of free nitric acid. This, the only fluid preparation of mercury officially recognized, is made by solution of 40 Gm. of mercuric oxide in a mixture of 45 Gm. of nitric acid and 15 Gm. of water. According to the equation $3HgO + 8HNO_3 = 3Hg(NO_3)_2 + 2NO + 4H_2O$, 643.14 parts of mercuric oxide require 500.56 parts of absolute nitric acid to form 964.92 parts of mercuric nitrate; hence 40 Gm. will require 31.13 Gm. of absolute, or 45.78 Gm. of official, nitric acid and will yield 60.32 Gm. of the salt. Moderate dilution of the acid with water is advantageous, facilitating the solution of the newly formed salt.

This very corrosive preparation, rarely used, and then only for external application, requires great care in handling. It is also known by the name acid nitrate of mercury, and is the densest solution of the Pharmacopœia, having a specific gravity of 2.086 at 25° C. (77° F.).

Among the non-official compounds of mercury of interest to the pharmacist, the following may be mentioned:

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potassium tartrate, the univalent group SbO, known as antimonyl, replacing the hydrogen in the acid potassium tartrate, water being formed at the same time.

The synonyms tartar emetic and tartrated antimony are largely used for this compound, the former being the name generally employed in commerce. The salt is recognized in the British Pharmacopœia as *antimonium tartaratum*, and in the German Pharmacopœia as *tartarus stibiatus*. It is generally sold in powder form, obtained by trituration of the crystals. Aqueous solutions of tartar emetic gradually develop fungi, and on that account cannot be kept on hand for any length of time, nor can they be mixed with strongly alcoholic liquids without precipitation, as the salt is totally insoluble in alcohol.

The Pharmacopœia requires almost absolute purity (99.5 per cent.) for tartar emetic, the valuation being made with $\frac{N}{10}$ iodine solution in the presence of sodium bicarbonate and starch solution. The iodine, acting as an oxidizing agent, converts the antimonyl into meta-antimonic acid, hydriodic acid and sodio-potassium tartrate being also formed; the object of adding sodium bicarbonate is to neutralize the two newly formed acids, thereby preventing decomposition of the hydriodic acid by the meta-antimonic acid, which would liberate iodine and thus vitiate the end-reaction. The official directions to begin titration immediately after addition of the sodium bicarbonate solution are intended to prevent the separation of antimonous oxide, caused by action of the alkali bicarbonate on the antimony and potassium tartrate, a reaction known to occur if the two salts are kept together in solution for some time. The equation $(2K(SbO)C_4H_4O_6 + H_2O) + I_4 + 8NaHCO_3 = 2NaSbO_3 + 4NaI + 2KNaC_4H_4O_6 + 8CO_2 + 5H_2O$ shows that each molecule (or 659.8 parts) of crystallized tartar emetic requires 4 atoms (or 503.6 parts) of iodine for complete oxidation of the antimony present; hence 0.33 Gm. at 99.5 per cent. or 0.32835 Gm. will require 0.25060 + Gm. of iodine or 19.9 Cc. of its tenth-normal solution, for $659.8 : 503.6 :: 0.32835 : x$ ($x = 0.25060$), and $0.25060 \div 0.01259 = 19.9$.

The following compounds of antimony are no longer recognized in the U. S. Pharmacopœia, but are official in the British Pharmacopœia, and therefore deserving of consideration: antimony oxide, purified antimony sulphide, and sulphurated antimony.

Antimony Oxide. Antimonous Oxide. Antimony Trioxide. Sb_2O_3.—This compound is obtained by first preparing a solution of antimony trichloride, $SbCl_3$, from antimonous sulphide and hydrochloric acid, pouring this into water, whereby antimony oxychloride, $2SbCl_3 + 5Sb_2O_3$ (known as powder of Algaroth), is precipitated, which is then repeatedly washed with water and mixed with a solution of sodium carbonate, converting the oxychloride into pure oxide, with elimination of carbon dioxide and formation of sodium chloride; thus, $(2SbCl_3 + 5Sb_2O_3) + 3Na_2CO_3 = 6Sb_2O_3 + 6NaCl + 3CO_2$. In place of sodium carbonate, ammonia water is frequently employed. After proper washing of the oxide it is dried at a temperature not exceeding 100° C. (212° F.), so as to avoid the formation of higher oxides.

Antimony oxide is used in the manufacture of tartar emetic and antimonial powder. The latter preparation is official in the British Pharmacopœia, and is made by mixing 1 part of antimony oxide thoroughly with 2 parts of calcium phosphate.

Purified Antimony Sulphide. Sb_2S_3.—Although the official Latin name of this compound is given in the British Pharmacopœia as *Antimonium Nigrum Purificatum*, the official English name is simply *Antimonous Sulphide*. It is made by macerating finely divided native antimony sulphide, preferably obtained by elutriation, for several days in a closed vessel with diluted ammonia water, with frequent agitation; the liquid is then decanted and the residue repeatedly washed with water and dried at a gentle heat. Antimonous sulphide is always associated with arsenous sulphide, which it is intended to remove by the treatment with ammonia water, wherein it is soluble. Hager and others suggest that ammonium carbonate be added to the mixture, after two or three days' maceration, with a view of dissolving less of the antimonous sulphide, which, although soluble to some extent in the ammonia water, is totally insoluble in solution of ammonium carbonate.

Purified antimony sulphide differs in appearance from the crude sulphide, being a lustreless powder of dark-gray or grayish-black color.

Sulphurated Antimony.—This preparation is defined in the British Pharmacopœia to be a mixture of antimony sulphides and oxides with some sulphur. Commercially it is often designated as *golden sulphuret of antimony* or *golden sulphur*, and is recognized in the German Pharmacopœia as *stibium sulphuratum aurantiacum*, the German name being *Goldschwefel*, which is identical with golden sulphur. Sulphurated antimony, as recognized abroad, is not identical with the sulphurated antimony or Kermes Mineral, formerly official in our Pharmacopœia. The directions for its manufacture are to boil for two hours a mixture of purified antimony sulphide and sulphur with solution of sodium hydroxide, whereby sodium sulphide is formed which, reacting with sulphur and antimonous sulphide, yields sodium sulphantimonate, a compound known as Schlippe's Salt—thus, $Sb_2S_3 + S_2 + 3Na_2S = 2Na_3SbS_4$; some antimonous oxide is also formed by action of the alkali and remains mixed with the other precipitate obtained when diluted sulphuric acid is added to the solution of sodium sulphantimonate, which consists almost wholly of antimony pentasulphide; the resulting hydrogen sulphide escapes, and sodium sulphate remains in solution, as shown by the equation $2Na_3SbS_4 + 3H_2SO_4 = Sb_2S_5 + 3H_2S + 3Na_2SO_4$. The presence of antimony trisulphide is due to possible formation of sodium sulphantimonite during the boiling of the alkaline mixture, and its subsequent decomposition by the acid.

THE COMPOUNDS OF ARSENIC.

Arsenous Iodide. AsI_3.—Arsenic is capable of forming several compounds with iodine, of which, the one indicated by the above formula and more particularly known as arsenic triiodide, is alone recognized in the Pharmacopœia. It may be obtained by fusing, in a loosely stoppered test-tube or bottle, a mixture of 4 Gm. of metallic arsenic and 20 Gm. of iodine, and pouring the melted mass on a porcelain slab to cool. Some manufacturers prefer to make it by adding finely powdered metallic arsenic to a solution of iodine in carbon disulphide until all color of iodine has disappeared, then concentrating and crystallizing the solution.

In the official test, demanding that not less than 21.9 Cc. of $\frac{N}{10}$ iodine solution shall be required to impart a slight yellow color to a solution of 0.5 Gm. of arsenous iodide and 2 Gm. of sodium bicarbonate in 50 Cc. of water, it is but proper to assume that the arsenous iodide, well known to be rather unstable, is decomposed with the formation of sodium arsenite and sodium iodide, as shown by the equation $AsI_3 + 5NaHCO_3 = 3NaI + Na_2HAsO_3 + 5CO_2 + 2H_2O$; this being the case, the titration with iodine solution is analogous to that of solution of potassium arsenite. The reaction $Na_2HAsO_3 + I_2 + H_2O = Na_2HAsO_4 + 2HI$ indicates that each molecule of sodium arsenite, corresponding to 1 atom of metallic arsenic, requires 2 atoms of iodine for complete oxidation, and hence each Cc. of $\frac{N}{10}$ iodine solution, representing 0.01259 Gm. of iodine, corresponds to 0.00372 Gm. of metallic arsenic, for $251.8 : 74.4 :: 0.01259 : 0.00372$. If 21.9 Cc. of iodine solution are required for the 0.5 Gm. of arsenous iodide, these will correspond to 21.9×0.00372 or 0.081468 Gm. of metallic arsenic, which is equivalent to 16.29 + per cent. of the 0.5 Gm. of arsenous iodide taken, as required by the Pharmacopœia. In the official test each Cc. of $\frac{N}{10}$ iodine solution used will represent 0.744 per cent. of metallic arsenic.

Arsenous iodide must be carefully protected from air and light, otherwise it undergoes decomposition, losing iodine and becoming insoluble in water. Its aqueous solution gradually changes, arsenous and hydriodic acids being formed. The chief use made of the compound is in the preparation of the official solution of arsenous and mercuric iodides, also known as Donovan's Solution.

Arsenic Trioxide. As_2O_3.—This compound has been known for centuries, and although it is still designated as arsenous acid by some Pharmacopœias, the names arsenic trioxide, or arsenous anhydride, seem more in conformity with its true character, since the dry substance evinces no acid properties whatever, and shows only a feeble acid reaction even when dissolved in water. It is obtained chiefly as a by-product in the roasting of tin, cobalt, and nickel ores, and is subsequently purified by sublimation.

Arsenic trioxide occurs in two distinct varieties, an amorphous, vitreous (glass-like) form and a crystalline, opaque, porcelain-like variety, the former being gradually converted into the latter upon exposure to moist air. The solubility of the two varieties in water differs materially, the vitreous being nearly three times as soluble as the porcelain-like variety, but the solubility of both is increased by the presence of hydrochloric acid or alkali hydroxides and carbonates, alkali arsenites being formed in the last two cases. When arsenic trioxide is dissolved in water arsenous acid is formed; thus, $As_2O_3 + 3H_2O = 2H_3AsO_3$, which, however, cannot be isolated, as upon evaporation of the solution arsenic trioxide is again obtained. While alcohol exerts but a slight solvent effect on either variety, glycerin will dissolve about one-fifth of its weight of both, again depositing a portion however upon dilution with water, and oil of turpentine dissolves the vitreous but not the opaque variety.

Although the synonym *white arsenic* is frequently applied, it should be borne in mind that the commercial product in powder form, known as white arsenic, is often impure and unfit for pharmaceutical purposes. Arsenic trioxide should never be purchased in powder form, except in bottles bearing on the label the name of some reputable manufacturer or dealer.

The quality of arsenic trioxide can be readily ascertained by titration with tenth-normal iodine solution, which converts arsenous into arsenic acid. The Pharmacopœia requires that official arsenic trioxide shall contain not less than 99.8 per cent. of As_2O_3; 0.1 Gm. dissolved in 20 Cc. of water together with 1.0 Gm. of sodium bicarbonate should decolorize at least 20.3 Cc. $\frac{N}{10}$ iodine solution, the following reaction taking place: $As_2O_3 + 8NaHCO_3 + I_4 + 2H_2O = 2Na_2HAsO_4 + 4NaI + 8CO_2 + 5H_2O$. Since 1 molecule (or 196.68 parts) of arsenic trioxide requires 4 atoms (or 503.6 parts) of iodine for complete oxidation, each Cc. of $\frac{N}{10}$ iodine solution must correspond to 0.004911 Gm. As_2O_3, and 20.3 Cc. equal 0.0996933 Gm., which is 99.7 per cent. of 0.1 Gm. The addition of sodium bicarbonate is made for the purpose of neutralizing the acids formed, thus preventing the constant liberation of iodine through decomposition of the hydriodic acid by the arsenic acid.

The official method of determining the purity of arsenic trioxide is not very desirable on account of the long time required to effect perfect solution of the arsenic trioxide in the presence of sodium bicarbonate, and should be modified by adding to the hot mixture of arsenic trioxide and water small portions of a 10 per cent. solution of sodium hydroxide until solution is complete, after which the liquid is exactly neutralized by means of normal sulphuric acid.

20 Cc. of a saturated solution of sodium bicarbonate may then be added and the titration with iodine carried out in the usual manner.

Solution of Arsenous Acid.—This is simply a solution of arsenous acid in water, containing also 5 per cent. of official diluted hydrochloric acid, which latter is added solely to facilitate solution of the arsenous oxide, no chemical action taking place. Formerly this preparation was called solution of chloride of arsenic, under a false impression; arsenous chloride, As_2Cl_6, can be obtained by treating arsenic trioxide with strong hydrochloric acid, but upon being dissolved in water it is again split up into the componnds from which it was made.

The Pharmacopœia requires that the solution shall contain in every Cc. 0.010 Gm. of official arsenic trioxide as arsenous acid (corresponding to about 4.57 grains in every fluidounce), which is determined by titration with $\frac{N}{10}$ iodine solution, as in the case of the valuation of arsenic trioxide. 24.6 Cc. of the official solution, containing 0.2455 Gm. of absolute As_2O_3 (1 Gm. of 99.8 per cent. arsenic trioxide in 100 Cc.) will require not less than 50 Cc. $\frac{N}{10}$ iodine solution, each Cc. of which corresponds to 0.004911 Gm. As_2O_3, for complete oxidation. The reaction has been fully explained in the preceding article.

Solution of Arsenous and Mercuric Iodides.—Red mercuric iodide, which alone is almost insoluble in water, becomes soluble in the presence of arsenous iodide, and in preparing the above solution the two iodides are triturated together and then mixed with water, when solution readily takes place. It is important that the arsenous iodide be of good quality, otherwise an insoluble residue will remain. The solution contains in every Cc. 0.010 Gm. each of arsenous and mercuric iodides (corresponding to about 4.57 grains of each in every fluidounce), and should be preserved in small, well-stoppered vials, in a dark place, as it is prone to decompose. When freshly made, it is of a pale straw-color, and, if this changes to reddish or red, iodine has been liberated, and the solution should not be dispensed.

This preparation is better known as Donovan's Solution, and was at one time considered a valuable remedial agent, but is little used at present. On account of the powerful action of arsenous and mercuric iodides this solution was formerly called by some physicians *The Three Samsons of Medicine.*

Solution of Potassium Arsenite.—This preparation, popularly known as Fowler's Solution, is probably the most extensively employed of all arsenical compounds. It is made by heating arsenic trioxide and potassium bicarbonate with a small quantity of water until perfect solution has been effected, which when cold is diluted with water, and compound tincture of lavender added. The use of a small quantity of water is favorable to chemical union between the alkali and feeble acid. The exact nature of the compound in solution is somewhat in doubt, some authorities believing that when one molecule of arsenic trioxide and four molecules of acid potassium carbonate are brought together with water, as in the official process, secondary potassium ortho-arsenite, K_2HAsO_3, is formed according to the equation $As_2O_3 + 4KHCO_3 = 2K_2HAsO_3 + 4CO_2 + H_2O$; others claim that primary potassium ortho-arsenite, KH_2AsO_3, is produced; while still others assert that potassium meta-arsenite, $KAsO_2$, only is formed, as in the preparations of the British and German Pharmacopœias made with equal weights of arsenic trioxide and normal potassium carbonate.

The solution is most conveniently prepared in a small, long-neck flask, whereby the evaporation of water is materially lessened; the dilution should not be made until the liquid is cold. Solution of potassium arsenite is likely to develop fungi in the course of time, and if an excess of alkali be present, as in the British and German preparations, the arsenous acid is gradually converted into arsenic acid; it is better, therefore, not to keep the solution on hand in large quantities. While the preparations of the United States and British Pharmacopœias are colored reddish by the compound tincture of lavender added, those of the German and French Pharmacopœias are colorless. The term *liquor arsenicalis* is officially used in Great Britain to designate this solution.

Owing to its very poisonous nature, Fowler's Solution should never be dispensed without a physician's prescription, and, although sometimes called for by the public, pharmacists should refuse to sell it, for their own protection as well as that of others.

The official solution of potassium arsenite must contain 1 Gm. of official arsenic trioxide in combination in every 100 Cc. of solution, corresponding to 4.57 grains in each fluidounce, which is determined with iodine exactly as in the case of solution of arsenous acid.

Solution of Sodium Arsenate.—An aqueous solution of sodium arsenate, containing 0.010 Gm. of anhydrous salt in each Cc. The object of using anhydrous sodium arsenate is to insure uniformity of strength in the finished product, as the commercial salt may contain variable proportions of water of crystallization (see page 502); the temperature used for desiccation should not be carried beyond 149° C. (300° F.), in order to avoid changing the sodium ortho-arsenate into pyro-arsenate.

This preparation is not identical with Pearson's Arsenical Solution, recognized in the French Pharmacopœia, and prepared by dissolving 1 part of crystallized sodium arsenate in 600 parts of water. As Pearson's Solution is sometimes prescribed in this country, it should be borne in mind that the solution of sodium arsenate of the United States Pharmacopœia is about ten times as strong as the French preparation bearing Dr. Pearson's name. The *National Formulary* states that Pearson's Solution may be made by mixing 1 volume of the official solution of sodium arsenate with 9 volumes of distilled water.

THE COMPOUNDS OF BISMUTH.

Bismuth Citrate. $Bi_6C_6H_5O_7$ or $C_3H_4(CH)(COO)_3Bi$.—This salt is prepared by heating a mixture of 100 Gm. of bismuth subnitrate and 70 Gm. of citric acid, with 400 Cc. of water, on a boiling water-bath, until a drop of the mixture forms a clear solution with ammonia water, after which it is diluted with a large volume of water, allowed to subside, and repeatedly washed with water by decantation until free from nitric acid, and dried with the aid of a gentle heat.

The use of a small quantity of water is advantageous for the complete conversion of the bismuth subnitrate into citrate; the reaction taking place may be illustrated by the following equation: $(BiONO_3 + H_2O) + (H_3C_6H_5O_7 + H_2O) = BiC_6H_5O_7 + HNO_3 + 3H_2O$, which shows that 100 Gm. of bismuth subnitrate require 68.98 Gm. of crystallized citric acid (for 302.23 : 208.5 : : 100 : 68.98), which leaves a very slight excess of citric acid in the official formula. The composition of bismuth subnitrate may differ, however, from the formula assigned to it in this reaction (see Bismuth Subnitrate).

The Pharmacopœia requires that bismuth citrate after ignition and treatment with nitric acid, shall, when again ignited, leave a residue of bismuth oxide amounting to not less than 58 nor more than 60 per cent. As 2 molecules of bismuth citrate are capable of yielding 1 molecule of bismuth oxide, Bi_2O_3, the theoretical yield should be 58.48 per cent.

The only use made of the normal bismuth citrate in pharmacy is in the manufacture of the soluble compound next mentioned.

Bismuth and Ammonium Citrate.—The official formula for this preparation directs that ammonia water shall be gradually added to a smooth paste made of normal bismuth citrate and twice its weight of water, until a perfect solution has been effected, which is strained, concentrated on a water-bath to a syrupy consistency, and spread upon plates of glass to dry. A slight excess of ammonia water will be advantageous in order to maintain a neutral or faintly alkaline reaction during evaporation of the solution, as some ammonia will be lost and an acid condition would cause precipitation.

The exact composition of this compound cannot be definitely stated. By some the view is held that by the action of ammonia bismuthous hydroxide is formed, which is held in solution by the ammonium citrate simultaneously produced, giving the salt the composition indicated by the formula $Bi(OH)_3 + (NH_4)_3C_6H_5O_7 +$ Aq.; others have suggested that the composition may be expressed thus: $BiC_6H_5O_7 + NH_4OH + H_2O$.

If bismuth and ammonium citrate be treated exactly as stated under Bismuth Citrate, the Pharmacopœia requires that the yield of oxide shall not be less than 48 per cent., which corresponds very nearly to a salt having the composition indicated by the first formula given above, the theoretical yield of which would be 46.25 per cent., whereas a salt indicated by the second formula would yield over 51 per cent.

The scaled salt obtained by the official process slowly loses ammonia unless preserved in tightly stoppered bottles, thereby becoming opaque and partly insoluble in water. When such a condition exists, the cautious addition of a few drops of ammonia water to the turbid mixture usually effects a perfect solution, as in similar cases of the iron scale-salts.

The British Pharmacopœia recognizes a solution of bismuth and ammonium citrate, which is prepared by dissolving 40 grains of normal bismuth citrate in 1 fluidounce of water by means of ammonia. It is prepared as described above, and is known in England also as *liquor bismuthi*.

Bismuth Subcarbonate. Bismuthyl Carbonate.—The first step necessary in the manufacture of this compound is the preparation of a solution of pure normal bismuth nitrate, which is then decomposed by means of a cold solution of sodium carbonate. When metallic bismuth is treated with nitric acid, a solution of bismuth trinitrate, $Bi(NO_3)_3$, is formed, and the arsenic which is almost invariably present in bismuth is converted into arsenic acid, and combining with bismuth forms bismuth arsenate, $BiAsO_4$. In order to rid the solution of the latter salt it is diluted with water to incipient turbidity and set aside for twenty-four or thirty-six hours, when nearly all the bismuth arsenate will have been deposited, being less soluble than the nitrate; by adding an excess of ammonia water to the clear solution all bismuth will be precipitated as bismuthous hydroxide, ammonium nitrate and arsenate remaining in solution. After washing the precipitate until the washings are tasteless, it is redissolved in nitric acid, and the resulting solution of purified bismuth trinitrate slowly added, with constant stirring, to a solution of alkali carbonate, when the following reaction occurs: $2Bi(NO_3)_3 + 3Na_2CO_3 + H_2O = (BiO)_2CO_3 + H_2O + 6NaNO_3 + 2CO_2$. The final precipitate, consisting of basic bismuth carbonate, is thoroughly washed with water and dried with moderate heat.

The exact composition of bismuth subcarbonate depends upon the degree of dilution of the sodium carbonate solution and the temperature at which the bismuth nitrate is added and the final precipitate dried. The Pharmacopœia demands that bismuth subcarbonate, upon being heated to redness, shall leave a yellow residue of bismuth oxide, Bi_2O_3, weighing not less than 90 per cent. of the original weight of the sample used; a salt of the above composition will yield 88.02 per cent. of oxide, whereas the formula given by the British Pharmacopœia, $2(Bi_2O_2CO_3) + H_2O$, indicates a salt which will yield 89.75 per cent. of oxide. In England the salt is known as bismuth carbonate or bismuth oxycarbonate, the British Pharmacopœia directing the use of ammonium carbonate in place of sodium carbonate.

Bismuth Subgallate. Bismuthyl Gallate.—This compound, commercially also known as *dermatol*, may be obtained by dissolving bismuth trinitrate in glacial acetic acid, diluting the solution with water, and adding, with constant stirring, a warm, weak aqueous solution of gallic acid. The resulting precipitate is separated by decantation and washed until entirely free from nitric acid, and then dried at about 100° C. (212° F.). Its composition may be indicated by the formula $BiOC_7H_5O_5 + H_2O$ or $C_6H_2(OH)_3COOBiO + H_2O$, but it varies somewhat in commercial samples. Bismuth subgallate occurs as a bright yellow powder, insoluble in water, but soluble in solutions of the alkali hydroxides.

The Pharmacopœia requires that if thoroughly ignited and then treated exactly as stated under Bismuth Citrate, it shall yield not less than 52 nor more than 59 per cent. of pure bismuth oxide; the theoretical yield of a compound having the above composition would be 54.33 per cent.

Bismuth Subnitrate. Bismuthyl Nitrate.—A part of the process of manufacture of this salt has been detailed. When a solution of purified bismuth trinitrate is poured into water precipitation of a basic salt at once takes place, the nitric acid liberated, however, retaining some of the normal nitrate in solution. As in the case of the carbonate, the composition of the precipitate will vary with the volume and temperature of the water used, and also the temperature at which the salt is dried.

The Pharmacopœia gives no formula for bismuth subnitrate, but demands that it shall yield not less than 80 per cent. of bismuth oxide, if heated to redness until nitrous vapors cease to be evolved and then weighed when cold. The British Pharmacopœia gives $BiO(NO_3) + H_2O$ as the composition of the official salt, which would yield a little over 76 per cent. of oxide, while the formula $BiO(NO_3) + H_2O + Bi(OH)_3$ indicates a compound theoretically yielding somewhat over 82 per cent.

Although a basic salt, bismuth subnitrate, when mixed with water, shows an acid reaction, due to decomposition and liberation of nitric acid, and should not be dispensed in mixtures containing alkali carbonates or bicarbonates, as decomposition (often with explosive violence) will result (see also page 329).

In continental Europe the salt is frequently prescribed under the name *magisterium bismuthi.*

Bismuth Subsalicylate. Bismuthyl Salicylate.—$BiOC_7H_5O_3$ or $C_6H_4(OH)COOBiO$. According to the British Pharmacopœia, which names this salt bismuth salicylate, it may be prepared by interaction between bismuth nitrate and sodium salicylate. Another method consists in digesting freshly precipitated bismuth hydroxide with salicylic acid at ordinary temperature for 48 hours, then washing with small quantities of cold water until all free acid has been removed, and finally drying at a low temperature in a dark place.

The Pharmacopœia requires that if bismuth subsalicylate be ignited and treated exactly as stated under Bismuth Citrate, it shall yield not less than 62 nor more than 64 per cent. of oxide, which corresponds to a salt having the composition given above.

Among the non-official compounds of bismuth the following are of interest:

Bismuth Oxide. Bi_2O_3.—This compound may be conveniently prepared by boiling bismuth subnitrate with solution of potassium or sodium hydroxide, washing the resulting precipitate well with water, and finally drying it on a boiling water-bath. It is officially recognized in the British Pharmacopœia. Bismuth oxide is of yellowish-white color, and is used in the preparation of bismuth oleate.

Bismuth Subiodide. Bismuthyl Iodide. BiOI.—This salt is obtained either by boiling an aqueous suspension of bismuth subnitrate with potassium iodide or by heating, but not boiling, a solution of normal bismuth nitrate with potassium iodide. In either case the bright red or brownish-red precipitate is well washed with water and dried at the temperature of boiling water.

CHAPTER LII.

THE COMPOUNDS OF COPPER, LEAD, ZINC, GOLD, AND SILVER.

WHILE copper and gold each furnish but one compound recognized in the Pharmacopœia, the official salts of lead, silver, and zinc are more numerous and of greater importance, as may be seen by the following list:

Official English Name.	Official Latin Name.
Copper Sulphate,	Cupri Sulphas.
Lead Acetate,	Plumbi Acetas.
Lead Iodide,	Plumbi Iodidum.
Lead Nitrate,	Plumbi Nitras.
Lead Oxide,	Plumbi Oxidum.
Lead Plaster,	Emplastrum Plumbi.
Cerate of Lead Subacetate,	Ceratum Plumbi Subacetatis.
Solution of Lead Subacetate,	Liquor Plumbi Subacetatis.
Zinc Acetate,	Zinci Acetas.
Zinc Bromide,	Zinci Bromidum.
Precipitated Zinc Carbonate,	Zinci Carbonas Præcipitatus.
Zinc Chloride,	Zinci Chloridum.
Zinc Iodide,	Zinci Iodidum.
Zinc Oxide,	Zinci Oxidum.
Zinc Phenolsulphonate,	Zinci Phenolsulphonas.
Zinc Stearate,	Zinci Stearas.
Zinc Sulphate,	Zinci Sulphas.
Zinc Valerate,	Zinci Valeras.
Solution of Zinc Chloride,	Liquor Zinci Chloridi.
Ointment of Zinc Oxide,	Unguentum Zinci Oxidi.
Ointment of Zinc Stearate,	Unguentum Zinci Stearatis.
Gold and Sodium Chloride,	Auri et Sodii Chloridum.
Silver Cyanide,	Argenti Cyanidum.
Silver Nitrate,	Argenti Nitras.
Mitigated Silver Nitrate,	Argenti Nitras Mitigatus.
Moulded Silver Nitrate,	Argenti Nitras Fusus.
Silver Oxide,	Argenti Oxidum.

THE COMPOUNDS OF COPPER.

Copper Sulphate. $CuSO_4 + 5H_2O$.—The [illegible] salt known as [illegible] article may be obtained by direct solution of metallic copper in diluted sulphuric acid aided by a little nitric acid, the following reaction taking place: $Cu_3 + 3H_2SO_4 + 2HNO_3 = 3CuSO_4 + 2NO + 4H_2O$. The solution may be concentrated and allowed to crystallize or evaporated with frequent stirring, so that the salt will be obtained in the form of a coarse granular powder, which latter is more convenient for dispensing purposes.

The official crystallized cupric sulphate, containing 36.1 per cent. of water, slowly effloresces upon exposure to air; hence it must be kept in tightly closed vessels. When deprived of all of its water of crystallization at a temperature of 200° C. (392° F.), the anhydrous salt forms a valuable dehydrating agent and is used in the preservation of absolute alcohol.

Among the non-official compounds of copper the following may be mentioned as of interest to pharmacists:

Copper Arsenite. $CuHAsO_3$.—This salt, which of late years has come somewhat into prominence, is obtained as a green precipitate by decomposing a solution of cupric sulphate with potassium arsenite.

Copper Acetate. $Cu(C_2H_3O_2)_2 + H_2O$ or $(CH_3COO)_2Cu + H_2O$.—Crystallized cupric acetate, which was recognized in the Pharmacopœia of 1880, may be obtained by double decomposition of cupric sulphate and lead or calcium acetate; the solution after filtration is acidulated with acetic acid, concentrated, and allowed to crystallize. This salt must not be confounded with ordinary verdigris, a basic cupric acetate, which occurs in amorphous masses and has the composition $Cu_2O(C_2H_3O_2)_2$.

Copper Nitrate. $Cu(NO_3)_2 + 3H_2O$.—A very deliquescent salt prepared from metallic copper by solution in diluted nitric acid and subsequent crystallization.

Copper Alum.—By this name the German Pharmacopœia recognizes a mixture of alum, saltpetre, cupric sulphate, and camphor, which has received also the official Latin title *cuprum aluminatum.* It is prepared by fusing together 16 parts each of potassium alum, cupric sulphate, and potassium nitrate, and adding to the fused mixture, after removal from the fire, 1 part each of powdered camphor and powdered potassium alum; after thorough incorporation of the powders the mass is poured on a slab to solidify. This mixture is sometimes prescribed by physicians as *lapis divinus.*

THE COMPOUNDS OF LEAD.

Lead Acetate. $Pb(C_2H_3O_2)_2 + 3H_2O$ or $(CH_3COO)_2Pb + 3H_2O$.—This salt may be obtained by dissolving lead in diluted acetic acid or by exposing lead in the form of sheets to the combined action of air and vinegar. The resulting solutions are filtered, concentrated, and crystallized; in order to secure perfect crystallization a little acetic acid is added to the liquid. Large quantities of lead acetate are now made from metallic lead by placing the same in granular form in large open stoneware cylinders and allowing strong acetic acid to fall upon it in drops from a cask provided with a glass outlet tube and a multiple drip-cock attachment. During the operation, which is allowed to go on continuously day and night until completed, heat is developed as the acid slowly trickles down over the metal, and under the influence of air the lead is gradually dissolved in the form of basic lead acetate. The solution is allowed to collect in the lower part of the cylinder, and is thence transferred to large receptacles, where it is exactly neutralized with acetic acid, and the solution of normal lead acetate then set aside to crystallize. Purified lead acetate for dispensing purposes is prepared in granular form by dissolving the large crystals in water, filtering and evaporating the solution with frequent stirring, so that small crystals may be produced.

Commercially, lead acetate is better known as sugar of lead, on account of its peculiar sweet taste. When exposed to the air it effloresces and slowly absorbs carbon dioxide; it must therefore be preserved in well-closed bottles or cans.

Lead Iodide. PbI_2.—This salt is prepared by double decomposition between cold solutions of lead nitrate and potassium iodide; the precipitate is well washed with water and dried at a gentle heat. Lead acetate may be used in place of the nitrate, but entails a loss of the product, since lead iodide is appreciably soluble in potassium acetate solution.

Lead iodide may be adulterated with lead chromate, which resembles it in appearance; such an admixture can be detected by treatment with a hot solution of ammonium chloride, in which lead iodide is soluble, while lead chromate remains unaffected.

Lead Nitrate. $Pb(NO_3)_2$.—While metallic lead is soluble in diluted nitric acid, lead oxide or carbonate is preferred for the manufacture of this salt, as solution can be effected more readily; the solution of lead nitrate thus obtained is concentrated and crystallized. Lead nitrate is insoluble in alcohol, and in this respect differs from lead acetate, which is soluble in 30 times its weight of that liquid.

Lead Oxide. PbO.—Of the different oxides of lead occurring on the market, only that more particularly known as litharge is officially recognized. It is obtained by heating lead in contact with air to a temperature of about 400° to 450° C. (752° or 842° F.), and also as a by-product in the treatment of silver ores by the process known as cupellation.

When lead oxide is exposed to the air it slowly absorbs moisture and carbon dioxide, a basic lead carbonate being formed; hence it should be kept in well-closed vessels; the Pharmacopœia limits the increase in weight due to such absorption to 2 per cent. The color of commercial litharge is not uniform, which is due to the manner of cooling the molten mass: if allowed to cool slowly, a reddish-yellow product is obtained; while if cooled rapidly, a yellowish-red color results.

Solution of Lead Subacetate.—An aqueous liquid containing in solution not less than 25 per cent. of basic lead acetate of the approximate composition $Pb_2O(C_2H_3O_2)_2$. The official directions for preparing this well-known solution are to boil for half an hour a mixture of 180 Gm. of lead acetate, 110 Gm. of lead oxide, and 700 Gm. of distilled water, with occasional stirring. When cool, the mixture is filtered and sufficient distilled water, previously boiled and cooled, added to the filtrate to bring the weight of the latter up to 1000 Gm.

The lead acetate should be dissolved in the distilled water heated to boiling and then added to the lead oxide in the form of finely sifted powder, in divided portions, and slowly with constant stirring. After a thorough mixture has been effected it is then boiled for half an hour to complete the chemical reaction. Distilled water, preferably that which has been boiled, so as to avoid the presence of carbon dioxide, as well as sulphates and chlorides, should always be used in the preparation of this solution. The process of boiling the mixture is directed mainly for the purpose of economizing time, as the same changes will take place even at ordinary temperature, several days, however, being required, together with frequent agitation of the vessel.

The quality of solution of lead subacetate depends largely upon the quality of the lead acetate and lead oxide employed. The following process, suggested by Haussmann, is admirably adapted for the retail pharmacist's needs, and yields a more satisfactory product than the official method; pour 730 Cc. of distilled water, heated to boiling, into a strong bottle previously warmed and graduated at 730 Cc.; add quickly 170 Gm. of pure crystallized lead acetate in small pieces, cork the bottle, and dissolve by gentle agitation. After solution of the salt, add in divided portions 100 Gm. of lead oxide (97–99 per cent. pure), previously sifted, shaking the bottle after each addition. In about ten minutes the yellow color of the lead oxide will disappear, and after two hours all reaction will have ceased. The mixture may then be filtered under cover.

Several basic lead acetates are known, the composition of which depends upon the proportions in which the lead acetate and oxide are employed; thus the United States and British Pharmacopœias, using the acetate and oxide in the proportion of their molecular weights, obtain in solution the basic compound indicated by the formula $Pb_2O(C_2H_3O_2)_2$, according to the equation $(Pb(C_2H_3O_2)_2 + 3H_2O) + PbO = Pb_2O(C_2H_3O_2)_2 + 3H_2O$; while the German and French Pharmacopœias, directing the use of three parts of lead acetate to one of lead oxide, cause the production of a less basic compound, as shown by the equation $2(Pb(C_2H_3O_2)_2 + 3H_2O) + PbO = Pb_3O(C_2H_3O_2)_4 + 6H_2O$.

In the preparation of this solution other basic lead acetates, such as $Pb_3O_2(C_2H_3O_2)_2$, are also formed in small quantities in addition to those mentioned, and an insoluble white residue is always left, consisting of a very basic compound, probably having the composition $Pb_6O_5(C_2H_3O_2)_2$.

Solution of lead subacetate, commercially known as Goulard's Extract, is very sensitive to carbon dioxide, the least exposure to air causing a film of basic lead carbonate to form; hence it must be preserved in tightly stoppered bottles, and should always be filtered in a closely covered funnel. It is incompatible with solution of acacia, differing in this respect from the normal acetate.

The valuation of solution of lead subacetate is made by precipitating all lead present by addition of an excess of $\frac{N}{10}$ oxalic acid solution, and then determining the excess of oxalic acid by means of potassium permanganate solution. From the data thus obtained the percentage of lead subacetate in the solution may be calculated. In the official test 10 Gm. of solution of lead subacetate are diluted with recently boiled and cooled distilled water to 100 Cc., and of this diluted liquid 13.6 Cc., representing 1.36 Gm. of the original solution, are added to 35 Cc. of $\frac{N}{10}$ oxalic acid solution, and, after thorough shaking, sufficient distilled water is added to bring the volume up to 50 Cc., the mixture again well shaken, and after the precipitate has settled 10 Cc. of the clear liquid are diluted with 50 Cc. of distilled water, and after addition of 2 Cc. of sulphuric acid titrated with $\frac{N}{10}$ potassium permanganate solution. Not more than 2 Cc. of the latter solution should be required to produce a permanent pink tint. The reaction occurring in the assay may be shown by the the following equation: $Pb_2O(C_2H_3O_2)_2 + 2(H_2C_2O_4 + 2H_2O) = 2Pb(C_2O_4) + 2HC_2H_3O_2 + 5H_2O$, from which it is seen that every molecule or 543.74 Gm. of lead subacetate will require 2 molecules or 250.20 Gm. of crystallized oxalic acid; and hence each Cc. of the $\frac{N}{10}$ oxalic acid solution, containing 0.006255 Gm. of the acid, will precipitate 0.01359 + Gm. of lead subacetate, which corresponds practically to 1 per cent. of the 1.36 Gm. of original solution taken. The number of Cc. of $\frac{N}{10}$ potassium permanganate solution required to produce the permanent tint must be multiplied by 5, since only $\frac{1}{5}$ of the clear supernatant liquid is used, and this product subtracted from 35 will indicate the exact quantity of $\frac{N}{10}$ oxalic acid solution required to precipitate all lead from 1.36 Gm. of the solution taken for the assay. The number of Cc. of the oxalic acid solution thus required will at once express the percentage of lead subacetate present, since each Cc. indicates 1 per cent.

The Pharmacopœia also recognizes a dilute solution of lead subacetate, made by mixing 40 Gm. of the above solution with 960 Gm. of distilled water, previously boiled and cooled. This preparation is popularly known as lead water.

THE COMPOUNDS OF ZINC.

Zinc Acetate. **$Zn(C_2H_3O_2)_2 + 2H_2O$ or $(CH_3COO)_2Zn + 2H_2O$.**—This salt may be prepared by solution of either zinc oxide or carbonate in hot, moderately diluted acetic acid. After filtration the solution is allowed to cool, when a large portion of the newly formed salt separates. A further yield of crystals may be obtained by concentration of the mother-liquor. It is better to crystallize the salt from a slightly acid solution, so as to avoid the formation of basic zinc acetate.

Zinc acetate upon exposure to air slowly effloresces and loses acetic acid, a basic salt being formed at the same time; hence it should be preserved in well-stoppered bottles.

Zinc Bromide. **$ZnBr_2$.**—The most convenient method for preparing this salt is digestion of pure granulated zinc with a solution of hydrobromic acid as long as reaction continues, then filtering and evaporating the solution to dryness. Zinc bromide may, however, also be obtained by mutual decomposition between zinc sulphate and potassium bromide or by the direct action of bromine on metallic zinc in the presence of water.

Zinc bromide is a very deliquescent salt, and must therefore be kept in bottles closed with glass stoppers coated with paraffin. The Pharmacopœia requires that the salt when perfectly dry shall contain at least 97 per cent. of pure zinc bromide, and hence in the official test 0.3 Gm. should require not less than 26 nor more than 26.8 Cc. of $\frac{N}{10}$ $AgNO_3$ solution for complete precipitation, potassium chromate being used as indicator. As 1 molecule of zinc bromide requires 2 molecules of silver nitrate for precipitation, each Cc. of the silver solution, containing 0.016869 Gm. of silver nitrate, is capable of precipitating 0.011181 Gm. of zinc bromide, which is equivalent to 3.727 per cent. of 0.3 Gm., and hence it will require 26 Cc. to indicate 97 per cent. of 0.3 Gm., for $97 \div 3.727 = 26.0+$; moreover, 97 per cent. of 0.3 is 0.291, and $0.291 \div 0.011181 = 26$. If the salt should be absolutely pure, 0.3 Gm. will require 26.83 Cc. of the silver solution, and the difference between 26.83 and 26 Cc. may be due to a higher percentage of purity or to the presence of chloride, the latter condition being more likely.

Precipitated Zinc Carbonate.—This amount is obtained by mutual decomposition between zinc sulphate and sodium carbonate. On mixing cold solutions of these two salts normal zinc carbonate is precipitated in a gelatinous form, but rapidly undergoes decomposition, carbon dioxide being liberated, whereby a portion of the precipitate is again dissolved. If, however, the solution of zinc sulphate be added slowly and with constant stirring to a boiling solution of sodium carbonate, carbon dioxide is rapidly expelled and a basic zinc carbonate precipitated; thus, $5(ZnSO_4 + 7H_2O) + 5(Na_2CO_3 + 10H_2O) = (2ZnCO_3 + 3Zn(OH)_2) + 5Na_2SO_4 + 3CO_2 + 82H_2O$; the mixture is boiled for a short time, after which the precipitate is washed with water until all sodium sulphate is removed, and then dried at a gentle heat. Potassium carbonate is not so well adapted as the sodium salt for the process, as the resulting potassium sulphate is less readily washed out, and ammonium carbonate is unsuitable, since it does not completely precipitate the zinc.

The composition of commercial zinc carbonate will naturally vary with the particular process employed in its manufacture and the relative proportions of the two salts used. The British Pharmacopœia assigns the formula $ZnCO_3 + 3Zn(OH)_2 + H_2O$ to the official article, thereby indicating a more basic compound than the one above mentioned.

The Pharmacopœia makes no statement as to the composition of the official zinc carbonate, but requires that it shall, upon strong ignition, yield at least 72 per cent. of zinc oxide. Such a compound is indicated by the formula of the British Pharmacopœia, which will yield theoretically 72.7+ per cent. of pure oxide.

Impure native zinc carbonate, contaminated with iron, is known in commerce as calamine, and was at one time used in the preparation of Turner's Cerate (calamine 3 parts, yellow wax 3 parts, lard 16 parts.

Zinc Chloride. $ZnCl_2$.—This salt may be obtained by evaporating the official solution of zinc chloride to dryness, with constant stirring, adding toward the close of the operation a little hydrochloric acid to avoid, as far as possible, the formation of oxychloride. Owing to the very hygroscopic character of the salt, it must be transferred while still warm to perfectly dry bottles, which should be closed with paraffined glass stoppers.

The entire absence of basic salt in zinc chloride is scarcely possible, and the Pharmacopœia prescribes the limit by directing that 1 drop of hydrochloric acid shall clear up the opacity caused in 5 Cc. of a 5 per cent. aqueous solution of the salt by the addition of an equal volume of alcohol. If flocculi are observed in a solution of zinc chloride, they are evidence of the presence of oxychloride, and should be removed by the cautious addition of dilute hydrochloric acid. As zinc chloride acts destructively upon vegetable fibre, strong solutions of it should always be filtered through asbestos or glass wool.

The Pharmacopœia demands that the official salt shall contain 99.5 per cent. of pure $ZnCl_2$, which is determined by ascertaining the yield of zinc oxide obtainable from a given weight of the chloride, and should be not less than 59.4 per cent. Each Gm. of absolutely pure zinc chloride is capable of yielding 0.5972+ Gm. of zinc oxide, and hence in the official test 0.5 Gm., if the salt be 99.5 per cent. pure, should yield 0.2971+ Gm. The reactions involved in the official test are precipitation of the zinc chloride as basic zinc carbonate, conversion of this into zinc nitrate by solution in nitric acid, and reduction of the nitrate to oxide by ignition.

Zinc Iodide. ZnI_2.—This salt can be prepared by direct union of iodine and zinc in the presence of water, when zinc iodide will be formed with liberation of hydrogen. The solution thus obtained is evaporated, with constant stirring, to dryness, the resulting salt resembling zinc bromide in appearance. Upon exposure to air zinc iodide is gradually oxidized, iodine being liberated and the salt becoming colored; hence it must be kept in small, tightly stoppered vials; like the bromide, it is also very deliquescent.

Zinc iodide should contain not less than 98 per cent. of pure ZnI_2, which is ascertained by means of silver nitrate and potassium sulphocyanate solutions in the presence of nitric acid and ferric ammonium sulphate solution, as is customary for the titration of iodides. In the official test not less than 31 nor more than 31.6 Cc. of $\frac{N}{10}$ $AgNO_3$ solution shall be required for precipitation of 0.5 Gm. of zinc iodide. The lower limit will indicate 98 per cent. purity, since each Cc. of the silver solution corresponds to 0.015835 Gm. of zinc iodide and 0.015835 × 31 = 0.490885 Gm., which is equivalent to 98 per cent. of 0.5 Gm. If the salt be absolutely pure, 0.5 Gm. will require 31.57+ Cc. of the silver solution for precipitation, and the difference between 31 and 31.6 Cc. required may therefore be due to a higher percentage of purity, or to the presence of bromide or chloride, or both.

Zinc Oxide. ZnO.—For pharmaceutical purposes zinc oxide is usually obtained by heating precipitated zinc carbonate in a crucible until all carbon dioxide and water have been expelled, the process being identical with that for the production of magnesia; thus $2ZnCO_3 + 3Zn(OH)_2 = 5ZnO + 2CO_2 + 3H_2O$. A red heat is not necessary, decomposition taking place at a temperature of 250° or 280° C. (482° or 536° F.). The lower the temperature employed for expelling the carbon dioxide the whiter will be the oxide obtained, a full red heat always causing a decided yellow tint.

The Pharmacopœia demands almost absolute purity for zinc oxide, 99.5 per cent., which is determined by dissolving 1 Gm. of the sample in an excess of normal hydrochloric acid (30 Cc.) and then titrating the excess with normal potassium hydroxide solution; not more than 5 Cc. of the alkali solution should be required, showing that at least 24.6 Cc. of the normal acid have been required to dissolve the zinc oxide. The equation $ZnO + 2HCl = ZnCl_2 + H_2O$ shows that 1 molecule, or 80.78 Gm. of zinc oxide, requires 2 molecules or 72.36 Gm. of absolute hydrochloric acid, or, in other words, that 1 Cc. of the normal acid, containing 0.03618 Gm. of absolute acid, is capable of dissolving 0.04039 Gm. of zinc oxide, which latter quantity corresponds to about 4 per cent. of the 1 Gm. used in the official test; hence 0.995 Gm. (99.5 per cent. of 1 Gm.) will require 24.63 Cc. to indicate 99.5 per cent. purity, for 0.995 ÷ 0.04039 = 24.63.

Zinc oxide is occasionally designated as *flores zinci* (flowers of zinc), *nihil album* (white nothing), or *lana philosophica* (philosopher's wool), and an impure gray variety was formerly used under the name *tutia* or *tutty.*

Zinc Phenolsulphonate. $Zn(C_6H_5O_4S)_2 + 8H_2O$ **or** $Zn(SO_3C_6H_4OH)_2 + 8H_2O$.—This salt, commercially better known as zinc sulphocarbolate, may be prepared by mutual decomposition between solutions of barium or lead phenolsulphonate (see Sodium Phenolsulphonate) and zinc sulphate, filtering the mixture, evaporating the clear solution, and allowing it to crystallize. As in the case of the corresponding sodium salt, the Pharmacopœia recognizes only the paraphenolsulphonate. The British Pharmacopœia recommends simple saturation of phenolsulphonic (sulphocarbolic) acid with zinc oxide. When freshly prepared the crystals of zinc phenolsulphonate are colorless, but are apt to become pink upon exposure to air and light, and should therefore be preserved in small tightly stoppered, amber-colored bottles. The salt effloresces when exposed to the air.

Zinc Stearate.—This compound, which is always accompanied by small but varying proportions of zinc palmitate, may be obtained by mutual decomposition between solutions of either zinc acetate or sulphate and sodium stearate, the latter being employed hot because the salt is not very soluble in cold water. 100 parts of zinc acetate or 131 parts of zinc sulphate will require 279 parts of sodium stearate; the latter may be procured in an impure form as animal or curd soap, or be prepared of purer quality by adding stearic acid to a hot solution of monohydrated sodium carbonate. The precipitated zinc stearate, after having been thoroughly washed with hot water, is dried between bibulous paper, reduced to powder, and passed through a hair-cloth sieve.

Zinc stearate has been found to retain its pulverulent condition very much better than zinc oleate, which was formerly much used and was often found mixed with zinc oxide for the purpose of better preservation.

The Pharmacopœia requires that 1 Gm. of zinc stearate, after decomposition with nitric acid and ignition of the newly-formed zinc nitrate, shall yield not less than 0.14 nor more than 0.16 Gm. of residue, indicating a zinc content corresponding to not less than 14 nor more than 16 per cent. of zinc oxide. An excessive weight of residue would indicate the probable admixture of zinc oxide.

Zinc Sulphate. $ZnSO_4 + 7H_2O$.—This salt is manufactured on a large scale by digesting metallic zinc with diluted sulphuric acid, when zinc sulphate is formed and hydrogen eliminated. As iron is generally present in zinc, this also is dissolved, and is removed by first converting it into a ferric salt (by passing chlorine into the solution) and afterward adding zinc carbonate, whereby all iron is precipitated as ferric hydroxide. The solution of zinc sulphate is separated by filtration, concentrated, and allowed to crystallize.

Commercial zinc sulphate frequently contains free acid, and is usually contaminated with iron and other metals; for pharmaceutical purposes only the purified salt in small crystalline granules should be used. On account of the acid reaction of an aqueous solution of zinc sulphate with litmus-paper, free acid to be detected must be extracted with alcohol, which has no effect on the salt, as directed in the Pharmacopœia.

Zinc Valerate. $Zn(C_5H_9O_2)_2 + 2H_2O$ or $((CH_3)_2CHCH_2COO)_2$-$Zn + 2H_2O$.—Formerly officially, and commercially still, named Zinc Valerianate. When hot solutions of sodium valerate and zinc sulphate are mixed, double decomposition takes place, sodium sulphate and zinc valerate being produced, the former of which remains in solution, while a portion of the zinc salt separates in the form of scaly crystals and rises to the surface; a further yield of crystals may be obtained upon concentration of the mother-liquor. The crystals are afterward drained, washed with small quantities of cold water, and dried at ordinary temperature.

Solution of Zinc Chloride.—An aqueous solution of zinc chloride, $ZnCl_2$, containing about 50 per cent. of the anhydrous salt. The official directions for preparing this solution are to digest metallic zinc with moderately diluted hydrochloric acid until the acid is saturated; the solution is decanted, and after the addition of a small quantity of nitric acid evaporated to dryness; the dry mass is next heated to fusion at a temperature not exceeding 115° C. (230° F.), allowed to cool and dissolved in sufficient water to bring the weight of the solution up to 1000 Gm. for every 840 Gm. of hydrochloric acid and 240 Gm. of zinc employed. Finally some zinc carbonate is added, the mixture agitated occasionally during twenty-four hours, allowed to settle, and the liquor decanted.

The object of adding nitric acid to the solution is to convert any iron present (derived from the zinc) into ferric chloride. To remove any nitrogen compounds or nitrate formed, the liquid is further evaporated to dryness and fused below 115° C. (230° F.), so as to avoid volatilization of any zinc chloride. The final addition of zinc carbonate precipitates all iron as ferric hydroxide, and thus a solution of zinc chloride only is obtained.

Solution of zinc chloride has a specific gravity of about 1.548 at

25° C. (77° F.), and is chiefly used for disinfecting purposes. It is practically identical with Burnett's disinfecting fluid.

Besides the foregoing compounds of zinc the following are of interest:

Zinc Hypophosphite. $Zn(H_2PO_2)_2 + H_2O$.—This salt may be conveniently prepared by dissolving zinc oxide or carbonate in hypophosphorous acid and allowing the solution to crystallize.

Zinc Lactate. $Zn(C_3H_5O_3)_2 + H_2O$ or $(CH_3CHOHCOO)_2Zn + 3H_2O$.—If moderately dilute lactic acid be neutralized with zinc carbonate, heating the mixture if necessary, and the resulting solution concentrated and set aside to cool, crystals of the above composition will be obtained.

Zinc Phosphate. $Zn_3(PO_4)_2 + 4H_2O$.—When a hot solution of zinc sulphate is added to a hot solution of official sodium phosphate, a white crystalline precipitate of zinc phosphate results, which is subsequently washed with water to remove all sodium salt and then dried at ordinary temperature.

Zinc Phosphide. Zn_3P_2.—Phosphorus and zinc may be made to unite by carefully adding small pieces of the former to fused zinc contained in a crucible, but it is difficult to obtain a product of uniform composition. A more desirable method for preparing the compound is that of Proust, whereby a mixture of hydrogen phosphide and nitrogen is passed into a porcelain tube containing metallic zinc heated to redness, the metal combining with the phosphorus, while the nitrogen and liberated hydrogen escape.

Zinc phosphide must be preserved in tightly stoppered vials, as upon exposure to air it slowly emits phosphorus vapor, indicating decomposition and oxidation.

Zinc Salicylate. $Zn(C_7H_5O_3)_2 + 3H_2O$ or $C_6H_4(OH)COO)_2Zn + 3H_2O$.—This salt may be conveniently obtained by gradually adding to a hot mixture of the salicylic acid and water an aqueous suspension of zinc oxide as long as solution is effected, which is then filtered and allowed to crystallize.

THE COMPOUNDS OF GOLD.

Gold and Sodium Chloride.—The official preparation is not the true double salt of the same name, but a mixture of gold chloride and sodium chloride. The double chloride of gold and sodium, known also as sodium chloroaurate, contains about 76 per cent. of pure auric chloride, whereas the official compound contains but 50 per cent. The exact composition of commercial gold and sodium chloride depends upon the mode of preparation; a simple mechanical mixture made by triturating sodium and gold chlorides together in equal proportions would be in conformity with the official definition.

Anhydrous auric chloride, $AuCl_3$, may be prepared by dissolving gold in nitromuriatic acid, evaporating the solution to dryness, dissolving the residue in water, and carefully evaporating the liquid to dryness at a temperature not exceeding 150° C. (302° F.); this operation is necessary to free the salt from acid, but a higher temperature must be avoided, lest decomposition of the auric chloride into aurous chloride and chlorine occur.

A solution of metallic gold in a mixture of nitric and hydrochloric acids contains chloroauric acid, according to the equation $Au_2 + 2HNO_3 + 8HCl = 2HAuCl_4$ or $2(AuCl_3 + HCl) + 2NO + 3H_2O$, and by adding to such a solution sodium chloride the double salt, sodium chloroaurate, is obtained upon evaporation; thus, $HAuCl_4 + NaCl = NaAuCl_4$ or $(AuCl_3 + NaCl) + HCl$. For the formation of this compound 5.187 parts of auric chloride require 1 part of sodium chloride; hence if equal parts of the two salts are used, a large excess of sodium chloride will be present.

The Pharmacopœia requires that the official compound shall contain an amount of gold chloride representing at least 30 per cent. of metallic gold, which is determined by adding an excess of potassium hydroxide solution to a solution of 0.5 Gm. of gold and sodium chloride, adding hydrogen dioxide solution, and heating the mixture for an hour on a waterbath. The precipitated metallic gold is well washed with water acidulated with hydrochloric acid, dried and ignited, and should then weigh not less than 0.15 Gm., which corresponds to at least 30 per cent. of the 0.5 Gm. taken. The reactions involved in the test may be indicated by the following equations: $2AuCl_3 + 12KOH = 2K_3AuO_3 + 6KCl + 6H_2O$ and $2K_3AuO_3 + 3H_2O_2 = 2Au + 3O_2 + 6KOH$.

Gold chloride being readily reduced by contact with organic matter, all such mixtures should be avoided; and as the official preparation is chiefly used in pill-form, non-oxidizable excipients only should be employed (see also page 346).

THE COMPOUNDS OF SILVER.

Silver Cyanide. $AgCN$.—This salt may be prepared either by passing freshly diluted hydrocyanic acid into a solution of silver nitrate or by adding a solution of the latter salt to a solution of pure potassium cyanide as long as a precipitate continues to be formed. In either case the precipitate must be well washed with water and dried in a dark place.

Silver cyanide becomes discolored upon exposure to light, and must therefore be kept in dark bottles. It is used in pharmacy solely for the extemporaneous preparation of diluted hydrocyanic acid.

The Pharmacopœia requires 99.9 per cent. purity for silver cyanide, which is conveniently determined by heating the salt in a porcelain crucible and weighing the metallic residue. As pure silver cyanide contains 80.54 per cent. of silver, the residue left after expulsion of the cyanogen should amount to 80.46 (80.459+) per cent. of metallic silver, provided the salt corresponds to the official requirements.

Silver Nitrate. $AgNO_3$.—This salt is preferably made from pure silver, and in order to obtain a product free from acid the metal is dissolved in nitric acid, the solution evaporated to dryness, the residue fused and redissolved in water, the solution filtered and allowed to crystallize. The evaporation to dryness and fusion of the residue are for the purpose of expelling any uncombined acid present, which, if the first solution were allowed to crystallize would to some extent be retained mechanically within the crystals: a temperature exceeding 200° C. (392° F.) must, however, be avoided, lest some of the silver nitrate be reduced to nitrite.

Silver nitrate is easily decomposed by contact with organic matter, and when exposed to light gradually assumes a gray color; hence proper precautions must be observed in keeping and dispensing it.

The Pharmacopœia requires absolute purity for crystallized silver nitrate, which is determined by titration with $\frac{N}{10}$ sodium chloride solution. An excess of the latter is added and then retitrated with $\frac{N}{10}$ $AgNO_3$ solution. The equation $AgNO_3 + NaCl = AgCl + NaNO_3$ shows that 168.69 parts of the silver salt require 58.06 parts of sodium chloride for complete precipitation; hence each Cc. $\frac{N}{10}$ NaCl solution corresponds to 0.016869 Gm. $AgNO_3$, and 0.5 Gm. of silver nitrate, as directed in the official test, if of 99.9 per cent. purity, will require not less than 29.6 (30 — 0.4) Cc. of the sodium chloride solution, for 99.9 per cent. of 0.5 is 0.4995, and $0.4995 \div 0.016869 = 29.61$.

Mitigated Silver Nitrate.—This preparation, also known as diluted silver nitrate, differs from the preceding in containing only 33.33 per cent. of pure silver nitrate, and being much milder in its action, is also known as mitigated caustic. It is made by fusing together 30 parts of silver nitrate and 60 parts of potassium nitrate, and, when a smooth, uniform mixture results, pouring the molten mass into suitable moulds, usually of a narrow cone shape.

The amount of pure silver nitrate present in any sample may be ascertained by means of $\frac{N}{10}$ sodium chloride solution, an excess of which is added and determined subsequently by retitration with $\frac{N}{10}$ silver nitrate solution, using potassium chromate as an indicator, as already explained in the preceding article. In the official test 1 Gm. of mitigated silver nitrate will require not less than 19.7 (20 — 0.3) Cc. of $\frac{N}{10}$ sodium chloride solution to conform to the requirement of $33\frac{1}{3}$ per cent. of pure silver nitrate, for $0.333 \div 0.016869 = 19.75$.

Moulded Silver Nitrate.—Under this name the Pharmacopœia recognizes a mixture of silver nitrate and chloride, containing 5 per cent. of the latter salt, and prepared by adding 1 part of hydrochloric acid to 25 parts of pure silver nitrate, melting the mixture at as low a temperature as possible and casting the mass in moulds. The object of converting a part of the silver nitrate into chloride is to render the resulting mass less brittle.

The synonym *lunar caustic*, given to this preparation in the U. S. Pharmacopœia, does not correspond with the same term commercially, which is usually applied to pure silver nitrate moulded into sticks, as also indicated in the British Pharmacopœia. The latter authority applies the name *toughened caustic* (argenti nitras induratus) to a mixture of 95 parts of silver nitrate and 5 parts of potassium nitrate.

The valuation of moulded silver nitrate is made exactly as in the case of mitigated silver nitrate. As it is required to contain not less than 94.8 per cent. of pure silver nitrate, at least 28.1 Cc. of $\frac{N}{10}$ sodium chloride solution will be required in the official test, for 94.8 per cent. of 0.5 is 0.4740, and $0.4740 \div 0.016869 = 28.1$. Like all silver salts, this one must also be protected from light to prevent discoloration.

Silver Oxide. Ag_2O.—This compound may be obtained by adding a solution of pure silver nitrate to a solution of potassium or sodium hydroxide, washing the resulting precipitate well with water, and finally drying the same on a water-bath. Ammonia water is not suitable for the process, since it forms a soluble compound with the oxide, having the composition $Ag_2O + NH_3$.

When ignited in a porcelain crucible silver oxide should yield 92.9 per cent. of its weight of metallic silver, corresponding to 99.8 per cent. of pure oxide. It is rarely employed in medicine at the present time, and should always be kept in dark amber-colored bottles to avoid reduction. It is quickly decomposed by oxidizing agents, and should never be triturated with organic substances.

ORGANIC SUBSTANCES.

UNDER this head are classified those many compounds of carbon, hydrogen, and oxygen, frequently associated with nitrogen, sulphur, phosphorus, and other elements, which are chiefly derived from the vegetable kingdom; a few are obtained also from the animal kingdom, and some are produced synthetically.

Prior to 1828, when Woehler announced to the scientific world the successful synthetic production of urea, an excretory product of the animal economy, solely from inorganic material, thereby establishing the intimate relationship between organic and inorganic matter, the agency of a peculiar vitalizing force was considered essential for the formation of all so-called organic bodies. No elements unknown to the mineral kingdom have ever been found in organic bodies, and the one feature which serves to distinguish this very large class of chemical compounds from those commonly designated as inorganic substances is the invariable presence of carbon; the term carbon compounds is therefore most appropriately applied to them.

The simplest form of carbon compounds are the hydrocarbons, composed exclusively of carbon and hydrogen; of these, two, methane, CH_4, and benzene, C_6H_6, may be said to be the source of all organic compounds, the constitution of which has thus far been studied and explained. The derivatives of these two hydrocarbons differ so widely in their properties that they have been conveniently grouped into two main classes, designated as fatty and aromatic compounds, respectively.

It is not within the scope of this book to enter into a detailed study of the so-called organic substances, and attention will be given only to those of pharmaceutical interest.

CHAPTER LIII.

CELLULOSE AND ITS DERIVATIVES.

All plants are made up of certain proximate principles, to which they owe their growth and value as nourishing or medicinal agents. The most widely diffused substance in the vegetable kingdom is cellulose or cell membrane, which goes to make up the body of all plants. During the growth and development of plants some of the cell membrane undergoes a change, becoming gradually hard and woody; to this modified form of cellulose the name lignin has been given, and the woody fibre of plants is assumed to be a combination of cellulose and lignin, called lignose. Cellulose and lignin being insoluble in all ordinary solvents, the chief object in pharmaceutical processes is to extract from them, by appropriate treatment, the many valuable principles they often enclose and upon which the medicinal value of vegetable drugs depends.

Lignin has not yet been obtained in a pure state, but pure cellulose has been isolated as a colorless, odorless, and tasteless gelatinous mass, which, upon drying, forms a horny substance, or may be obtained as a white powder. It is soluble in a solution of cupric hydroxide in ammonia water, known as Schweitzer's reagent, forming a mucilaginous fluid which, after dilution, admits of filtration, and, upon addition of an acid, is again precipitated. The elementary composition of pure cellulose corresponds to the formula $C_6H_{10}O_5$, or multiples thereof, as $C_{12}H_{20}O_{10}$ or $C_{18}H_{30}O_{15}$.

Cellulose is officially recognized in the form of gossypium, or cotton, and patent lint and paper are further examples of it. When heated with potassium or sodium hydroxide it is gradually converted into oxalic acid, alkali oxalates being formed, and, if boiled with diluted sulphuric acid, dextrin is produced, which is finally changed into dextrose, from which alcohol can be obtained by fermentation. Immersed in strong sulphuric acid, cellulose undergoes conversion into a substance called amyloid, upon which the preparation of parchment paper depends, the pores of the paper becoming filled with this modified cellulose, and thus made tough and impervious to water. Prolonged contact of the paper with strong sulphuric acid, however, is hurtful, the resulting product becoming friable; hence the best results are obtained if the paper be simply drawn through a mixture of two parts of concentrated sulphuric acid and one part of water, and then immediately well washed with water.

Official purified cotton, commercially known as absorbent cotton, is prepared by first boiling carefully carded cotton in a weak alkaline solution, for the purpose of removing fatty matter, after which it is rinsed in water and immersed in a weak solution of chlorinated lime. It is subsequently washed in water slightly acidulated with hydrochloric acid, and again well rinsed in water. If the cotton still retains fat, the treatment with alkali is repeated until the final product is found completely absorbent. For the more thorough removal of water after washing the cotton recourse is had to centrifugal machines, by means of which the material is rapidly dried.

Medicated cotton is usually prepared by impregnating absorbent cotton with a solution of the medicinal agent in alcohol and glycerin, and subsequently drying; the glycerin not being volatilized, serves as an adhesive agent for retaining the active ingredient on the fibre of the cotton. The solution is used of a definite strength and in such quantity that the whole of it will be absorbed by and saturate the material. Benzoated, borated, carbolated, iodized, salicylated, and other medicated cotton is prepared in this or a similar manner. The percentage of medicinal agent present must be calculated on the basis of finished product, irrespective of any adhesive agent that may have been employed, and which naturally forms a part of the finished product; thus, 25 Gm. of 10 per cent. borated cotton should contain 2.5 Gm. of boric acid, or 10 Gm. of 5 per cent. carbolated cotton should contain 0.5 Gm. of pure carbolic acid, etc. It has been suggested that impregnation of cotton with a 5 or 10 per cent. solution of any medicinal agent would constitute such cotton a 5 or 10 per cent. medication; but such an assumption is erroneous, since the absolute quantity of medicinal agent retained by the cotton must always be uncertain and variable in its relation to the weight of the finished product.

Cellulose and lignose both furnish most valuable pharmaceutical derivative products, the former by appropriate treatment with nitric acid, and the latter by dry distillation.

Pyroxylin.—Under this name the United States and British Pharmacopœias recognize a compound soluble in a mixture of alcohol and ether, and better known as collodion cotton, since it is used extensively in the preparation of collodion; the name colloxylin is also used as a synonym in this country. In Continental Europe the two terms are not considered synonymous, the name pyroxylin being applied to insoluble gun-cotton, and colloxylin to soluble collodion cotton. Pyroxylin is usually prepared by macerating purified cotton in a cooled mixture of 14 volumes of nitric acid and 22 volumes of sulphuric acid until the cotton has become soluble in a mixture of 1 volume of alcohol and 3 volumes of ether, then removing all adhering acid by washing first with cold and then with boiling water, and finally drying the product in small portions at a moderate heat (60° C. (140° F.).

When cotton is thoroughly imbued with strong nitric acid, cellulose nitrates and water are formed; thus, $C_6H_{10}O_5 + 2HNO_3 = C_6H_8(NO_3)_2O_3 + 2H_2O$. The exact character of the reaction depends upon the strength of the acid used, the temperature at which the cotton is immersed, and the length of time maceration is continued; thus, di-, tri-, tetra, penta-, and hexanitrate may be produced. The last two compounds are insoluble in alcohol and ether, and hence unfit for the purposes of official pyroxylin, which latter probably consists of a mixture of cellulose di- and trinitrate. It is important that the acids used be of official strength, and that the acid mixture, which becomes heated, be allowed to cool to 32° C. (90° F.) before the cotton is added, otherwise, in the latter case, the higher nitrates are formed and the staple of the cotton is destroyed; if weak acids be employed, prolonged maceration becomes necessary and imperfect nitration may result; in either case the product is insoluble.

In order that the cotton may be completely saturated with the acid mixture, it should be introduced in small portions, by the aid of a glass rod. The sulphuric acid used takes no part in the reaction, but facilitates the same by absorbing the water which is eliminated.

Pyroxylin was at one time looked upon as a nitro substitution-compound, and called nitrocellulose, the group NO_2 having been supposed to replace hydrogen in cellulose. Further studies of cellulose and the behavior of pyroxylin toward reagents have shown the latter compound to be a nitric acid ester or compound ether, formed by the displacement of hydrogen in the hydroxyl groups by the nitric acid radical, as shown by the formula $C_6H_8(ONO_2)_2O_3$ or $C_6H_7(ONO_2)_3O_2$. The correctness of this view is shown by the fact that nitric acid can be abstracted from cellulose nitrates by treatment with alkalies, and can also be completely displaced by concentrated sulphuric acid, even in the cold. All cellulose nitrates can be converted back into cellulose by reducing agents, and the degree of nitration can be definitely determined by treatment with ferrous sulphate and hydrochloric acid, the nitric oxide liberated being collected in a graduated tube, and from this the amount of nitric acid present can be calculated; the following equation explains the reaction: $2C_6H_7(ONO_2)_3O_2 + 18HCl + 18FeSO_4 = 2C_6H_{10}O_5 + 6NO + 6Fe_2(SO_4)_3 + 3Fe_2Cl_6 + 6H_2O$.

Pyroxylin is used in pharmacy exclusively in the preparation of plain and medicated collodion (see page 313), but has met with more extensive application in the arts in the manufacture of celluloid, a mixture of pyroxylin and camphor.

The Products of Distillation.—When wood is subjected to heat in air-tight cylinders or retorts a number of new substances are obtained, as a result of destructive distillation, the character of which depends largely upon the degree of heat employed and the care with which the process has been conducted. Both liquid and gaseous products are formed and distil over, when the solid residue is either charcoal or the original wood employed, but slightly altered in appearance. The liquid distillates include an acid fluid and tar; the former is known as pyroligneous acid or wood vinegar, which contains, besides acetic acid, acetone, C_3H_6O, methyl or wood alcohol, CH_3OH, furfurol, $C_5H_4O_2$, catechol or pyrocatechin, $C_6H_4(OH)_2$, and other substances.

Pyroligneous acid is not recognized in our Pharmacopœia, but is official in the German Pharmacopœia as *Acetum Pyrolignosum*, both the crude and rectified varieties being named. The former is described as a brown liquid containing at least 6 per cent. of acetic acid, and the latter as a yellowish liquid containing at least 5 per cent. of acetic acid; both liquids have a decided empyreumatic odor.

Acetic Acid. $HC_2H_3O_2$ or CH_3COOH.—Although this acid can be produced by oxidation of weak alcoholic liquids, it is obtained for the trade indirectly from wood.

Formerly much acetic acid was obtained in the form of wood-vinegar or pyroligneous acid, by destructive distillation of oak-wood in large iron retorts kept at a temperature of 205° C. (401° F.). This crude acid liquid, of slight yellowish color, was neutralized with soda-ash or sodium carbonate and evaporated, the resulting sodium acetate being then roasted to destroy empyreumatic products and to drive off water and other volatile matter. Upon finally treating the sodium acetate in suitable stills with sulphuric acid, purified acetic acid was obtained. This plan has, however, been abandoned by manufacturers, who now prefer to procure the acetic acid in the form of calcium acetate from charcoal-burners, and then bring this into solution and decompose it with sodium sulphate, whereby calcium sulphate is precipitated and sodium acetate remains in solution, which is then filtered and further treated as above explained.

If wood is distilled at temperatures above 230° C. (446° F.), as in the manufacture of charcoal, the resulting wood vinegar is more or less highly colored and possesses a strong empyreumatic odor. It requires a tedious process of purification by means of milk of lime, whereby soluble calcium acetate is formed and many impurities are precipitated as insoluble calcium compounds.

Chemically, acetic acid may be looked upon as methane or marsh-gas (CH_4), in which an atom of hydrogen has been replaced by the carboxyl group, COOH, forming a monobasic acid; thus, $CH_3COOH = HC_2H_3O_2$. It is a remarkably stable acid, and, although rich in oxygen, is not decomposed at moderately high temperatures, nor is it readily affected by oxidizing or reducing agents.

The Pharmacopœia recognizes three grades of acetic acid, which are officially designated as glacial acetic acid, acetic acid, and diluted acetic acid, and contain, respectively, 99, 36, and 6 per cent. of absolute $HC_2H_3O_2$. The three acids, recognized by the same names in the British Pharmacopœia, correspond very closely in strength to the above, containing 99, 33, and 4.27 per cent. of absolute acetic acid, respectively; but in the German Pharmacopœia the term acetic acid is used to designate a solution containing 96 per cent. of absolute acid, while the German diluted acetic acid contains 30 per cent.

Specific gravity is of no value in the examination of acetic acid, since the maximum density is reached in an 80 per cent. solution; beyond this point the specific gravity again decreases until absolute acetic acid is reached, having a density of 1.053. Official glacial acetic acid and an acid of 46 per cent. have the same specific gravity, 1.058, at 15° C. (59° F.), and, if diluted with water, the density of the weaker acid only will fall, that of the stronger acid increasing; between 73 and 84 per cent. acetic acid the specific gravity is almost stationary, the rise between these two points amounting to not more than 0.0008. Titration with normal alkali solution, as directed in the Pharmacopœia, is the only correct means of ascertaining the strength of acetic acid solutions, each Cc. of $\frac{N}{1}$ KOH solution corresponding to 0.05958 Gm. of absolute $HC_2H_3O_2$, as shown by the equation $KOH + HC_2H_3O_2 = KC_2H_3O_2 + H_2O$.

Glacial acetic acid is obtained by distilling anhydrous sodium acetate with highly concentrated sulphuric acid and exposing the resulting liquid to a temperature below 10° C. (50° F.); after crystallization has taken place the remaining liquid may be drained off and again exposed to cold to secure a further yield of crystals. Glacial acetic acid of official strength should retain its crystalline form until a temperature of at least 15° C. (59° F.) is reached, when it slowly begins to liquefy; some of the so-called glacial acetic acid of commerce is simply a strong solution, containing from 75 to 85 per cent. of absolute acid, and does not solidify at a temperature of 5° C. (41° F.) or even lower.

Glacial acetic acid readily absorbs moisture from the air and must therefore be preserved in tightly-stoppered bottles. At ordinary room-temperature it is a colorless liquid, but when the temperature falls below 15° C. (59° F.) it congeals to a crystalline mass and remains in that condition during cold weather. It has been employed as an excellent solvent for certain volatile oils, resins, and fatty bodies.

Official acetic acid is obtained, like the glacial acid, by distilling sodium acetate with sulphuric acid and finally adjusting the strength to the requirements of the Pharmacopœia. It should contain 36 per cent. of absolute acetic acid, and is used in pharmacy chiefly for the preparation of the official diluted acid, and also as an addition to the menstruum employed for tincture of sanguinaria and several extracts and fluidextracts.

Acetic acid for pharmaceutical purposes should be free from empyreuma, which may be detected by means of potassium permanganate, the color of which is readily discharged by empyreumatic substances. Upon neutralizing the acid with alkali and warming, no foreign odor should be perceptible.

Pharmacists will find it to their interest to purchase strong acetic acid and dilute this to suit their requirements, according to the rule given on page 73. Acetic acid of 60 and 80 per cent. strength can be purchased from reliable manufacturers at a relatively lower price than the official acid.

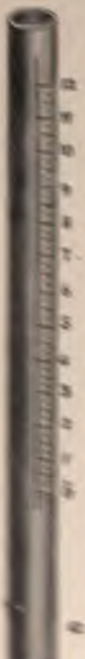
During the past ten years many experiments have been made with the view of utilizing acetic acid in place of alcohol for the extraction of aromatic, alkaloidal, and resinous principles from vegetable drugs. The results thus far have been satisfactory with some drugs, but wholly unsatisfactory with others, especially as regards the permanency of the finished product, and there is little probability of its extended use for the purpose intended. The Pharmacopœia, in an experimental way, has adopted the use of 10 per cent. acetic acid as a menstruum for 3 of the official fluidextracts, and also directs the same menstruum for extraction of nux vomica, in the preparation of the powdered extract of that drug, with the view of avoiding solution of the fatty constituents.

As the Pharmacopœia requires the official acetic acid to contain 36 per cent. of absolute $HC_2H_3O_2$, each Gm. of the acid will neutralize exactly 6 Cc. of normal potassium hydroxide solution. The commercial variety of acetic acid known as "No. 8" should never be used in place of the official acid, as it is weaker, containing only 30 per cent. of absolute acid.

Diluted acetic acid, recommended in the Pharmacopœia in place of commercial vinegar as a menstruum for several official preparations, is made by mixing 100 Gm. of the 36 per cent. acid with 500 Gm. of water, and contains, therefore, 6 per cent. of absolute $HC_2H_3O_2$. Its advantages over ordinary vinegar are purity and uniformity of strength, besides which the entire absence of color enables it to be used for colorless solutions, such as Spirit of Mindererus and the like.

While titration with normal alkali solution is always to be preferred as a means of ascertaining the strength of dilute solutions of acetic acid, other methods are also employed, such as neutralization with sodium or potassium bicarbonate, or with a standard ammonia solution in an instrument known as Otto's acetometer (see Fig. 296). The latter method is largely used in vinegar establishments, and gives results accurate to within 0.2 per cent. The acetometer consists of a graduated glass cylinder with rounded bottom, 36 centimeters (14 inches) in length and 2 centimeters (0.8 inch) internal diameter. The lower two graduations, marked a and b, indicate a volume of 1 and 10 Cc., respectively; while the upper part, from 1 to 12, is divided into 48 spaces, each equivalent to 0.52 Cc.; hence the large space between any two figures represents 2.08 Cc. The solution of ammonia used for the test contains 1.4 per cent. of absolute NH_3, and is prepared by mixing 14 Gm. of official 10 per cent. ammonia

FIG. 296.



Otto's acetometer.

water with 86 Gm. of distilled water; every 2.07 Gm. of the solution measures 2.08 Cc. and corresponds to 0.1 Gm. of absolute $HC_2H_3O_2$. When vinegar is to be tested, 1 Cc. of litmus test-solution is first poured into the tube, 10 Cc. of vinegar are then added, whereby the color of the litmus solution is changed to red, and finally sufficient of the above mentioned ammonia solution until, with gentle agitation, the blue color of the liquid is restored. From the volume of ammonia solution used, as shown by the graduated cylinder, the amount of absolute acetic acid present can readily be calculated.

Trichloracetic Acid. $HC_2Cl_3O_2$ or CCl_3COOH.—When chlorine is allowed to act on acetic acid, mono-, di-, and tri- substitution compounds are formed. The latter, known as trichloracetic acid, is official in the U. S. Pharmacopœia. It may be prepared by adding fuming nitric acid to fused hydrated chloral and setting the mixture aside until red vapors cease to be formed, after which it is distilled, that portion coming over above 190° C. (374° F.) and consisting of pure trichloracetic acid being collected.

Trichloracetic acid occurs in colorless deliquescent crystals, readily soluble in water, alcohol, and ether. It should be preserved in dark amber-colored, tightly-stoppered bottles. When mixed with $\frac{1}{10}$ its weight in water it forms a permanently liquid mixture. The acid is used as a cauterizing agent in minor surgery, but never employed internally.

Among the substances associated with acetic acid in crude wood vinegar are two of greater interest to pharmacists than the rest—acetone and methyl alcohol.

Acetone. C_3H_6O or CH_3COCH_3.—This compound, at one time also known as pyroacetic ether or pyroacetic spirit, was formerly obtained on a commercial scale solely by the destructive distillation of acetates (chiefly calcium acetate), but in 1895 a process was devised by the late Dr. E. R. Squibb for decomposing acetic acid vapor at a high temperature, between 500° and 600° C. (932° and 1112° F.), in a specially constructed iron rotary apparatus, whereby a large yield of fairly pure acetone may be secured. The crude acetone thus obtained is afterward purified by dehydration with caustic lime and redistillation. The decomposition of acetic acid vapor results in the formation of acetone and carbon dioxide, with the liberation of water; thus, $2HC_2H_3O_2 = C_3H_6O + CO_2 + H_2O$. The process and apparatus are fully described in *Ephemeris*, vol. iv., No. 3.

Chemically, acetone belongs to the class of compounds known as ketones, which consist of two alcohol radicals united by means of the bivalent group CO, called carbonyl; hence acetone is called also dimethyl ketone, and may be looked upon as acetic aldehyde, CH_3COH, in which a hydrogen atom is replaced by the methyl group.

Acetone is now extensively employed for the manufacture of chloroform, and has been found a valuable solvent for oleoresins, collodion cotton, etc. When pure it is a colorless, mobile, inflammable liquid of 0.790 specific gravity at 25° C. (77° F.), and boiling at 56.5° C. (133.7° F.). It is miscible in all proportions with water and alcohol, hence the commercial article is sometimes found contaminated with these substances. The Pharmacopœia demands not less than 99 per cent. purity, which is now readily obtainable.

Acetone is also used in the manufacture of certain chemical compounds, such as chloroform, iodoform etc., considered elsewhere. Besides these the following derivative is officially recognized:

Sulphonmethane. $\mathbf{C_7H_{16}S_2O_4}$ **or** $\mathbf{(CH_3)_2C(SO_2C_2H_5)_2}$.—Although the Pharmacopœia has, for the sake of more convenient brevity, adopted the present official title, the true chemical name of the compound is diethylsulphone-dimethylmethane. It is best known by its trade-name, under which it was first introduced into medicine, *sulphonal*, and is also recognized by this name in the British and German Pharmacopœias. The first step in its manufacture is the preparation of mercaptol or dithioethyl-dimethylmethane, $(CH_3)_2C(SC_2H_5)_2$, a condensation product obtained when dry hydrochloric acid gas is passed into a mixture of anhydrous acetone and anhydrous ethyl hydrosulphide (ethyl mercaptan), water being eliminated; thus $2C_2H_5SH + CO(CH_3)_2 = (CH_3)_2C(SC_2H_5)_2 + H_2O$. Mercaptol is an oily liquid of exceedingly disagreeable odor, which may be purified by washing with water and afterward with dilute solution of sodium hydroxide. Upon agitating mercaptol with a 5 per cent. potassium permanganate solution until the color of the latter remains, oxidation takes place and sulphonmethane is formed. The new product may be obtained absolutely pure by crystallization from water or alcohol.

Sulphonmethane occurs in the form of colorless, odorless, and nearly tasteless crystals, requiring 360 parts of water for solution at 25° C. (77° F.), but is soluble in 15 parts of boiling water.

Three compounds similar to sulphonal have been introduced as hypnotics, of which one is also recognized in the Pharmacopœia, *methonal*, *tetronal*, and *trional*. Methonal is chemically dimethylsulphone-dimethylmethane, $(CH_3)_2C(SO_2CH_3)_2$, and tetronal is diethylsulphone-diethylmethane, $(C_2H_5)_2C(SO_2C_2H_5)_2$; both are made like sulphonal, except that in the case of methonal methyl hydrosulphide is used in place of ethyl hydrosulphide, and in the case of tetronal, diethylketone is used in place of acetone. Trional is officially recognized under the name:

Sulphonethylmethane.—This compound is chemically diethylsulphone-methyl-ethylmethane, $(CH_3)(C_2H_5)C(SO_2C_2H_5)_2$, but is better known by its trade-name, trional. It is made exactly like sulphonal, except that acetone is replaced by methylethylketone, $CH_3COC_2H_5$. It differs from sulphonal chiefly in having a bitter taste and in being nearly twice as soluble in cold water, requiring 195 parts for solution at 25° C. (77° F.). Sulphonethylmethane is recognized in the German Pharmacopœia as *methylsulphonal.*

Methyl Alcohol. CH_4O or CH_3OH.—This compound, also known as wood alcohol and at one time called wood naphtha and pyroxylic spirit, may be obtained in a crude state by distilling wood vinegar after neutralization with sodium carbonate or milk of lime, and collecting the first portions coming over. Wood vinegar usually contains about 1 per cent. of methyl alcohol, and other more profitable sources are perhaps employed for commercial purposes. Methyl alcohol may be purified by heating in a water-bath with an excess of anhydrous calcium chloride, with which methyl alcohol forms a crystalline compound, $CaCl_2 + 4CH_3OH$, and, after all volatile matter has been dissipated, mixing the crystals with water and distilling, whereby the compound is split up and dilute methyl alcohol recovered, which is subsequently dehydrated with lime and redistilled. For some years a purified methyl alcohol, containing 97–98 per cent. of CH_3OH, has been offered under the name *Columbian Spirit,* but should never be used for pharmaceutical purposes on account of its toxic properties. Experiments made during the past five or six years have demonstrated that methyl alcohol does not act like ordinary or grain alcohol when administered internally, being eliminated less rapidly, and frequently causing blindness and other grave functional disturbances. Even when used in place of grain alcohol for the preparation of external remedies, it has been found to act as a poison, and hence is wholly unfit for use in pharmacy and medicine. As a fuel in spirit lamps it has been preferred on account of its lesser cost; for the same reason it is used in the place of grain alcohol for the preparation of varnishes and for other technical purposes, but unless highly purified it is even then objectionable, as its vapor has proven injurious to many persons.

Absolutely pure methyl alcohol is best prepared by distilling crystallized methyl oxalate with solution of potassium hydroxide and then dehydrating with lime; the cost of such an article is, however, two or three times as high as that of absolute ordinary or ethyl alcohol. Pure methyl alcohol boils at a comparatively low temperature, 66° C. (150.8° F.). Crude methyl alcohol has been used in England and Germany for the purpose of rendering ordinary alcohol unfit for other than technical uses, by mixing the two liquids; in Germany a further addition of allyl alcohol and acetone is prescribed. Ethyl alcohol thus mixed is known in England as methylated spirit, and in Germany as denaturated alcohol; it is not subject to excise tax.

Tar and its Derivatives.—Like wood vinegar, tar is a complex mixture containing different resins, oils, hydrocarbons, phenols, etc., and yields valuable medicinal products. Official tar is derived from pine wood, and is recognized in the Pharmacopœia as Pix Liquida, or liquid pitch; by distillation it yields the official oil of tar and a hard residue known as black pitch. One of the most important derivatives of wood tar is

Creosote.—This is a mixture of phenol-like bodies consisting chiefly of guaiacol and creosol. Beechwood tar is richer in creosote than that derived from other woods, containing usually about 5 per cent., and is therefore a more economical source. Upon distilling the tar a light and a heavy oily layer are obtained, together with an acid aqueous distillate; the heavy oil is subsequently treated with a concentrated solution of sodium carbonate, to remove acid constituents, and again distilled. That portion of the second distillate heavier than water, and consisting of impure creosote, is dissolved in a moderately strong solution of potassa or soda; any oily layer separating is removed, and the creosote precipitated by saturating the alkaline solution with sulphuric acid. The alternate treatment with alkali and acid is repeated until the alkaline solution is practically free from color and does not turn brown on heating. The precipitated creosote is finally washed with a weak alkaline solution and water, and distilled, that portion distilling between 200° and 220° C. (392°–428° F.) being collected.

As wood vinegar contains also small proportions of creosote, the latter is recovered therefrom by first separating the oily constituents by saturating the liquid with sodium sulphate, treating these with sodium carbonate solution, distilling, and proceeding as above.

When first distilled, creosote is colorless, but gradually assumes a yellowish tint, and, as found in commerce, is rarely free from color; upon exposure to air the color darkens materially. The so-called coal-tar creosote of commerce is unfit for medicinal use and should never be employed when creosote is called for. It consists chiefly of cresols (which see under Coal Tar Products), and unfortunately is sometimes offered as common creosote by unscrupulous dealers. For dispensing purposes only the official beechwood creosote should be employed, which may readily be distinguished from carbolic acid by its peculiar odor, its lesser solubility in water, its immiscibility with a mixture of glycerin and water, and other tests given in the Pharmacopœia; it does not congeal when cooled to —20° C. (—4° F.), but becomes gelatinous. Creosote is soluble in water to the extent of about 3 drops in a fluidounce, and whenever it is to be dispensed in solution in plain water or lime water the resulting mixture should invariably be passed through a pledget of cotton, as small particles of insoluble matter sometimes separate, particularly in the case of lime water mixtures.

The name creosote was given to this liquid on account of its power of preserving meat, and is derived from the Greek—*κρεας*, flesh, and *σωζειν*, to save, to preserve. Creosote was first separated from wood tar in 1832.

A number of non-official compounds of creosote have been introduced into medicine, such as creosote carbonate (creosotal), c. phosphate (phosote), c. tannate (creosal or tannosal), c. valerate or valerianate (eosote), which have met with varying favor, but do not appear deserving of discussion in this volume.

Guaiacol. **$C_7H_8O_2$ or $C_6H_4(OH)(OCH_3)$.**—This compound, chemically also known as methyl catechol, is the chief constituent of creosote, and upon which the medicinal value of the latter, no doubt, wholly depends. It is contained in creosote to the extent of from 60 to 90 per cent., and is obtained from it by fractional distillation, that portion distilling between 200° and 205° C. (392° and 401° F.) being collected as crude guaiacol; this is treated with ammonia to remove acid compounds and again distilled. The lower boiling fraction is collected, dissolved in ether, and treated with alcoholic solution of potassium hydroxide, which causes the separation of potassium guaiacol, $C_6H_4KOCH_3$, the latter being insoluble in ether. After thorough washing with ether the compound is crystallized from alcohol, decomposed by means of diluted sulphuric acid, and the liberated guaiacol again rectified. Guaiacol is not always found absolutely pure in commerce, the pure article occurring usually in a crystalline state, obtained by dissolving purified guaiacol in petroleum benzin, and then subjecting such a solution to spontaneous evaporation; the addition of a crystal of pure guaiacol facilitates crystallization.

Of late years synthetic guaiacol has been freely offered in crystals. It is made by heating in a tightly closed vessel a mixture of equal molecules of pyrocathechin, potassium hydroxide, and potassium methylsulphate, to a temperature of 170° to 180° C. (338°–356° F.), when the following reaction occurs: $C_6H_4(OH)_2 + KOH + KCH_3SO_4 = C_6H_4OHOCH_3 + K_2SO_4 + H_2O$. The resulting guaiacol may be removed by solution in alcohol or petroleum benzin and purified by recrystallization; or it may be made by heating a solution of metallic sodium, pyrocatechin, and methyl iodide in methyl alcohol; the resulting mixture is freed from methyl alcohol, the residue dissolved in sodium hydroxide solution, filtered, and decomposed by means of hydrochloric acid. The guaiacol thus liberated is distilled and then crystallized at a low temperature.

Guaiacol occurs both in the liquid and crystalline form, the former being the variety usually met with, as the crystals melt readily at 28.5° C. (83.3° F.), and will then remain liquid unless again exposed to a very low temperature. It is soluble in 53 parts of water at 25° C. (77° F.), and is readily soluble in alcohol, glycerin, ether, and acetic acid. When mixed with 10 volumes of sulphuric acid a pure yellowish color is produced, free from a reddish tint; the latter would indicate the presence of creosote. The Pharmacopœia also requires that guaiacol, when shaken with 2 volumes of petroleum benzin, shall remain clear and separate on standing into two distinct layers; it shall also form a white mass when heated with 2 volumes of sodium hydroxide solution and then cooled, the mass being soluble in 20 volumes of water.

While the name guaiacol is applied to the monomethyl ether of catechol, the dimethyl ether of catechol, $C_6H_4(OCH_3)_2$, is known as veratrol. It is a colorless, aromatic, oily liquid, having the same boiling-point as guaiacol and congealing to a crystalline mass when exposed to cold.

A number of derivatives of guaiacol have been introduced at various times, being chiefly compounds with acid radicals, such as guaiacol camphorate (guaiacamphol), g. carbonate, g. benzoate (benzosol), g. cinnamate (styracol), g. phosphate, g. phosphite, g. salicylate (guaiacol-salol), g. valerate or valerianate (geosote), etc., one of which is officially recognized.

Guaiacol Carbonate. $(C_7H_7O)_2CO_3$ or $(C_6H_4OCH_3O)_2.CO$.—This compound, also known as duotal, may be obtained by slowly passing carbonyl chloride, phosgene gas, $COCl$, into a solution of guaiacol in sodium hydroxide solution, sodium chloride and guaiacol carbonate being formed; the latter being insoluble is precipitated and washed subsequently with sodium hydroxide solution, after which it is crystallized from alcohol. It occurs as a white crystalline powder, melting between 84° and 87° C. (187.2° and 188.6° F.), and while insoluble in water, it is soluble in chloroform, ether, and alcohol, and to some extent in glycerin and fixed oils.

CHAPTER LIV.

COAL TAR PRODUCTS AND RELATED COMPOUNDS.

During the destructive distillation of coal, itself a modified form of wood, the result of slow decomposition caused by decay and fermentative action, gaseous as well as liquid products are obtained, besides a solid residue known as coke, the process being similar to that occurring in the distillation of wood. The gases are used extensively for illuminating and heating purposes, while the coal tar, which contains benzene, C_6H_6, toluene, C_7H_8, aniline, $C_6H_5NH_2$, naphthalene, $C_{10}H_8$, phenol, C_6H_5OH, cresol, C_7H_7OH, and other important substances, is further distilled, and furnishes, besides a solid residue, known as pitch or asphalt, a light and a heavy oil, from which the above compounds are extracted.

The distillate of coal tar, known as light oil, consists chiefly of hydrocarbons having various boiling-points, which can be separated from each other by fractional distillation. The most important of these is:

Benzene, C_6H_6, designated by many as benzol, which furnishes a number of valuable derivative products; it is obtained by collecting that portion of light oil distilling between 80° and 90° C. (176° and 194° F.), purifying the same by exposing it to a low temperature, when it crystallizes and is freed from adhering liquid impurities, and redistilling. The U. S. Pharmacopœia recognizes pure benzene among the official reagents and describes it as having a specific gravity of 0.871 at 25° C. (77° F.), congealing at 5.2° C. (41.3° F.), and boiling at 80.4° C. (176.7° F.). It is insoluble in water, but soluble in 4 parts of alcohol and in ether. Commercial benzol is recognized in the British Pharmacopœia, and there defined to be a mixture of about 70 per cent. of benzene and from 20 to 30 per cent. of toluene, having a specific gravity of 0.800 to 0.880 and boiling between 80° and 120° C. (176° and 248° F.).

Benzene must not be confounded with benzin, officially known as petroleum benzin, a mixture of hydrocarbons obtained by distillation from American petroleum (which see under Petroleum Products).

Toluene, or **Methylbenzene, $C_6H_5CH_3$,** is another hydrocarbon of interest to pharmacists as the source of the official benzosulphinide, considered below. It is obtained from the light oil of coal tar by fractional distillation, as a colorless, mobile liquid, resembling benzene, but differing from the latter in boiling at 110° C. (230° F.), and in not congealing even when cooled to —20° C. (—4° F.).

Naphthalene. $C_{10}H_8$.—This hydrocarbon, frequently also called naphthalin, exists, like benzene and toluene, in coal tar; it is found in the so-called heavy oil, and is deposited as a dark-colored crystalline substance from the fraction collected between 180° and 250° C. (356° and 482° F.). Crude naphthalene is purified by successive treatment with sodium hydroxide and sulphuric acid, to remove acid and basic by-products, after which it is repeatedly heated with concentrated sulphuric acid, being each time distilled with steam, and is finally resublimed. The white naphthalene thus obtained still has a tendency to darken when exposed to air and light, to overcome which it is treated for a short time with a mixture of sulphuric acid and manganese dioxide at water-bath temperature; finally, the product is washed with weak alkaline solution and water and again sublimed.

For pharmaceutical purposes, naphthalene recrystallized from alcohol should alone be used.

Aniline. $C_6H_5NH_2$.—This compound, also known as amidobenzene and phenylamine, occurs in small quantities in coal tar, but is chiefly manufactured from benzene by adding the latter in small portions to fuming nitric acid, when a dark red liquid is formed, from which, upon addition of water, an oily liquid is precipitated, known as nitrobenzene, $C_6H_5NO_2$. By the action of nascent hydrogen, subsequent mixture with milk of lime, and distillation, nitrobenzene is made to yield a basic fluid, to which the name aniline has been given.

While aniline itself is not used in medicine, it is of interest as furnishing a number of derivatives, both directly and indirectly. It is, when pure, a colorless, limpid, oily liquid, which soon acquires a yellow and finally a brown color when exposed to the air and light. Aniline is capable of forming salts with acids, which are mostly crystallizable.

Diphenylamine, $NH(C_6H_5)_2$, formed by heating aniline hydrochloride with aniline to 240° C. (464° F.), is used as a very delicate reagent for nitric acid, with which it strikes a deep blue color; the official test-solution is made by dissolving 0.1 Gm. of diphenylamine in 50 Cc. of diluted sulphuric acid.

Phenylhydrazine, $C_6H_5NH.NH_2$, is obtained by adding an aqueous solution of sodium nitrite to a solution of aniline in strong hydrochloric acid. To this liquid is added an acid solution of stannous chloride, and the resulting phenylhydrazine hydrochloride is then decomposed with an alkali and the base extracted with ether. It occurs in tabular crystals which melt at 17.5° C. (62.5° F.), and are only slightly soluble in cold water. Phenylhydrazine is used in the manufacture of antipyrine, and hence possesses more or less pharmaceutical interest.

Phenol. C_6H_5OH.—Although the name phenol has been officially adopted for this compound, it will probably continue to be known better by its former official, and still present commercial, name, carbolic acid. One of the reasons for changing the official title was the fact that a large number of impure products are offered as carbolic acid, and it was deemed wise to designate the official pure article intended for medicinal use by a specific name, universally applied to it by chemists. Chemically phenol is hydroxybenzene, and is the type of a class of compounds which are hydroxyl derivatives of the aromatic hydrocarbons, to which the class name phenols has been given.

Phenol occurs in that portion of the distillate from coal tar which comes over between 100° and 250° C. (212° and 482° F.), in proportions varying from 4 to 10 per cent. Besides the natural product, large quantities of phenol are also made synthetically.

Natural phenol may be obtained from the coal tar distillate named above by agitating the same with a 10 per cent. sodium hydroxide solution (a stronger solution is not desirable, since it would dissolve naphthalene and other impurities contained in the oil); upon standing, the mixture separates into two layers, the lower being a solution of sodium phenol, C_6H_5ONa, while the upper consists of the extracted oil. The lower layer is carefully drawn off and treated with hydrochloric or sulphuric acid in such quantity as has been ascertained (by a previous test) to be sufficient for exact decomposition. In some cases the sodium phenol solution, for the purpose of purification, is treated first with about one-eighth of the necessary quantity of acid, whereby homologous phenols are separated, and after the removal of these the solution is decomposed completely by acid. The impure phenol thus liberated rises as an oily layer to the surface, which, after removal, is washed by agitation with concentrated solution of common salt, freed from water by means of calcium chloride, and then distilled between 180° and 190° C. (356° and 374° F.). Upon exposure in cool places the distilled phenol congeals to a crystalline mass, which, after being freed from adhering liquid, is again distilled, that portion coming over below 185° C. (365° F.) being carefully collected and crystallized. Sometimes the phenol before final distillation is treated with potassium dichromate and sulphuric acid. In order to obtain phenol in colorless, loose crystals, it may be recrystallized from boiling petroleum benzin.

While the above method is the one now generally followed, some manufacturers extract phenol from a smaller fraction of the coal tar distillate, known as *heavy oil*, and collected between 160° and 220° C. (320° and 428° F.), the treatment being practically identical with that given above.

SYNTHETIC PHENOL.—Since 1888 considerable quantities of synthetic phenol have been placed upon the market. This is prepared directly from benzene by first treating it with fuming sulphuric acid and moderately warming the mixture, whereby benzenesulphonic acid is produced: $C_6H_6 + H_2SO_4 = C_6H_5SO_2OH + H_2O$.

The acid thus formed is neutralized with potassium carbonate, yielding potassium benzenesulphonate, and this compound then fused with a large excess of potassium hydroxide, whereby potassium sulphite and potassium phenol are formed: $2(C_6H_5SO_2OK) + 4KOH = 2H_2O + 2K_2SO_3 + 2C_6H_5OK$. The potassium phenol finally is treated in solution with hydrochloric acid, in order to liberate the phenol or carbolic acid, which is purified further by distillation: $C_6H_5OK + HCl = C_6H_5OH + KCl$. The advantages of the synthetic method are chiefly the absence of homologous products (cresol, xylene, etc.), as the benzene can be procured of great purity by means of crystallization.

Phenol occurs in crystalline masses and also in the form of loose crystals, having a faint aromatic odor, and should be free from color. It is freely soluble in glycerin and fixed oils; also in alcohol and ether, but requires about 20 parts of water for solution. The Pharmacopœia demands that if phenol be melted by aid of a gentle heat, and then slowly cooled with constant stirring until partly crystallized, the semicrystalline mass should have a temperature (remaining stationary for a short time) not lower than 40° C. (104° F.); the boiling-point of phenol should not be higher than 188° C. (370.4° F.). It must be borne in mind that cresols, which may be present, have a higher boiling-point, and that phenol may contain variable proportions of water, which would influence the congealing-point, and hence a lower boiling-point or a higher melting-point will indicate a purer and less hydrated phenol. The vapor of phenol is inflammable.

The Pharmacopœia demands that phenol shall contain not less than 96 per cent. of absolute C_6H_5OH, to be determined volumetrically by precipitation as tribromophenol, $C_6H_2Br_3OH$. The solution used for this purpose is known as Koppeschaar's Solution, and is designated in the Pharmacopœia as $\frac{N}{10}$ bromine solution, although it contains no free bromine; it is a solution of sodium bromate and bromide in such proportions that when treated with hydrochloric acid an amount of bromine is liberated corresponding to 0.007936 Gm. for each Cc. of the solution used, thus constituting it a $\frac{N}{10}$ bromine solution. In the official test an excess of this solution is added to an aqueous solution of phenol together with some hydrochloric acid, and the excess ascertained by addition of potassium iodide and subsequent titration of the liberated iodine by means of sodium thiosulphate solution. Since iodine is liberated by bromine in exact molecular proportions, 1 Cc. of $\frac{N}{10}$ sodium thiosulphate solution corresponds in value to 1 Cc. of $\frac{N}{10}$ bromine solution, and the number of Cc. $\frac{N}{10}$ $Na_2S_2O_3 + 5H_2O$ solution required to decolorize the iodine solution subtracted from the whole number of Cc. of $\frac{N}{10}$ bromine solution added originally, leaves the number of Cc. of the latter solution necessary for the precipitation as tribromophenol of all phenol present.

Four distinct reactions occur during the performance of this test before the data necessary for the calculation of the percentage of phenol present are obtained, namely: 1. The liberation of bromine by means of hydrochloric acid; thus, $NaBrO_3 + 5NaBr + 6HCl = 6NaCl + Br_6 + 3H_2O$. 2. The precipitation of tribromophenol; thus, $C_6H_5OH + Br_6 = C_6H_2Br_3OH + 3HBr$. 3. The liberation of iodine; thus, $2KI + Br_2 = 2KBr + I_2$ 4. The decoloration of the iodine solution; thus, $2(Na_2S_2O_3 + 5H_2O) + I_2 = 2NaI + Na_2S_4O_6 + 10H_2O$. The second equation shows that 93.34 parts of absolute phenol require 476.16 parts of bromine for complete precipitation; hence each Cc. of the bromine solution corresponds to 0.001556 Gm. of C_6H_5OH, for 476.16 : 93.34 : : 0.007936 : 0.001556. If 0.0389 Gm. of phenol be used as directed in the official test, 24 Cc. of $\frac{N}{10}$ bromine solution will be required to show 96 per cent. of absolute C_6H_5OH, each Cc. corresponding to 4 per cent., for 0.001556 is 4 per cent. of 0.0389 and $96 \div 4 = 24$; or 96 per cent. of $0.0389 = 0.037344$ and $0.037344 \div 0.001556 = 24$.

Phenol is a powerful poison, and many deaths have been recorded from swallowing the same, either accidentally or with suicidal intent. As an antidote alcohol has been found to act very effectually, especially in mitigating the caustic effects on the skin and mucous membranes. Oil or glycerin should never be administered after phenol has been swallowed, since both will facilitate absorption of the poison; sodium or magnesium sulphate is considered an efficient antidote, and alcohol, moderately diluted with water, is said to have been used with excellent results in carbolic acid poisoning.

The Pharmacopœia recognizes liquefied phenol under the title Phenol Liquefactum, which is prepared by melting phenol on a water-bath, and then adding for every 9 parts by weight of melted phenol, 1 part by weight of water, and mixing thoroughly. This liquid, if made from official phenol, contains 86.4 per cent. of absolute C_6H_5OH and 13.6 per cent. of water. It is soluble in 12 parts of water, and is miscible with alcohol, ether, and glycerin in all proportions, but on account of the water present will not mix clear with chloroform or olive oil. Liquefied phenol must be kept in a moderately warm room, since it will congeal to a crystalline mass at 13.5° C. (56.3° F.).

Cresol. C_7H_7OH or $C_6H_4(CH_3)OH$.—Under this name the Pharmacopœia recognizes a mixture of three isomeric bodies, which bear the same relation to toluene as phenol bears to benzene, being hydroxyl derivatives of that hydrocarbon. Commercially cresol is obtained from the coal-tar distillate collected between 140° and 220° C. (284° and 428° F.) by treatment with sodium hydroxide solution. By carefully adding to the solution thus produced some water and hydrochloric acid, hydrocarbons and tarry matter are removed, and the cresols precipitated by adding to the clarified filtrate a further limited quantity of hydrochloric acid, insufficient to liberate the phenol present, which latter remains in solution. The resulting product is redissolved in sodium hydroxide solution and again treated with acid as above, the precipitated liquid being finally fractionated by distillation between 180° and 200° C. (365° and 392° F.). This product is known as crude cresol; it is not recognized in our Pharmacopœia, but is official in Germany. By still further purification and distillation between 190° and 205° C. (383° and 401° F.), the official article is obtained.

Official cresol, also sometimes designated as tricresol, is a colorless or straw-colored refractive liquid, turning yellowish-brown on exposure to light and having a phenol-like odor. It is heavier than water and soluble in 60 parts of that liquid, and should form a clear solution with an equal volume of 10 per cent. sodium hydroxide solution. The chief constitutents are the three isomers, ortho-, meta- and paracresol, which boil respectively at 185°, 201°, and 198° C. (365°, 393.8° and 388.4° F.). All three possess strong antiseptic, germicidal, and disinfectant properties, and are far less poisonous than phenol.

Cresol is used in pharmacy for the preparation of the official Compound Solution of Cresol, which is made by adding cresol to an equal weight of linseed oil and potash soap, prepared from linseed oil 350 Gm., potassium hydroxide 80 Gm., and water 70 Gm. The mixture is stirred until a clear solution results. Compound solution of cresol is a yellowish-brown to brown saponaceous oily liquid and resembles some of the commercial products known as *creolin*, *lysol*, *sapocresol*, etc.

Crude cresol closely resembles the different grades of crude carbolic acid used for disinfecting purposes; some of the latter are often of very dark, almost black color, and contain considerable tarry matter.

Resorcinol. $C_6H_6O_2$ or $C_6H_4(OH)_2$.—Although the Pharmacopœia has changed the official name, of this compound somewhat, it is still known by its former name resorcin. It was first obtained by fusion of certain resins, such as those of ammoniac, galbanum, guaiac, etc., with potassium hydroxide, but is now made almost altogether from benzene by heating the latter with fuming sulphuric acid to 257° C. (494° F.), whereby benzene-metadisulphonic acid, $C_6H_4(HSO_3)_2$, is produced. This acid is neutralized with milk of lime and decomposed with sodium carbonate, and the solution of sodium benzene metadisulphonate thus obtained evaporated to dryness; the residue fused for several hours with sodium hydroxide yields sodium resorcin and sodium sulphite. Boiling an aqueous solution of the saline mass expels sulphurous acid, and, upon extracting the tar-like residue with ether and distilling, impure resorcinol is obtained, which is purified by sublimation and recrystallization from water.

Resorcinol is chemically known as metadioxybenzene, which shows it to be a diatomic phenol, $C_6H_4(OH)_2$; two isomerides are also known, namely, ortho- and paradioxybenzene, designated as catechol or pyrocatechin and hydroquinol or hydroquinone, respectively. The term resorcinol has also been applied to a proprietary preparation composed of equal parts of resorcinol and iodoform fused together, hence confusion is likely to arise.

Pure resorcinol occurs in colorless crystals, which readily assume a pink tint, and finally turn red upon exposure to air and light; it must, therefore, be carefully preserved, in tightly-stoppered bottles, in a dark place. Solutions of resorcinol also become rapidly colored, hence should always be dispensed in dark amber-colored vials.

Acetanilide. C_8H_9NO or $C_6H_5NHC_2H_3O$.—This compound, also known as phenylacetamide, is made direct from aniline, and hence is indirectly a benzene derivative. It is one of a class of chemical compounds known as anilides, which are derived from aniline by replacement of one or both hydrogen atoms of the amido group NH_2, by alcohol or acid radicals, hence both alcohol and acid anilides are known to chemists. Acetanilide is prepared by heating in a flask connected with a reflux condenser a mixture of equal parts of aniline and glacial acetic acid until a small portion of the mixture removed from the flask congeals on cooling; the mass is then distilled, when water and acetic acid first pass over, and afterward acetanilide, which is subsequently recrystallized from boiling water. The reaction involved in this process consists in the formation of aniline acetate, which upon heating is split up into acetanilide and water, as shown by the equations $C_6H_5NH_2 + HC_2H_3O_2 = C_6H_5NH_2HC_2H_3O_2$ and $C_6H_5NH_2HC_2H_3O_2 = C_6H_5NHC_2H_3O + H_2O$.

The name antifebrin has also been given to acetanilide; but being a proprietary name it has not officially been accepted as a synonym in most countries, although it is recognized in the Austrian Pharmacopœia. A compound closely allied to acetanilide is commercially known as *exalgine;* it is methylacetanilide, $C_6H_5NCH_3C_2H_3O$, and differs from acetanilide in having both hydrogen atoms of the amido group replaced, one by an alcohol radical and the other by an acid radical.

Acetphenetidin. $C_{10}H_{13}NO_2$ or $C_6H_4(OC_2H_5)NH.CH_3.CO$.—The true chemical name for this compound is acetparaphenetidin, which is recognized in the French and Austrian Pharmacopœias by the same name as in our own, but is called phenacetin in the British, German, and Swiss Pharmacopœias. It is indirectly a benzene derivative, being made from phenol by first acting on the same with diluted nitric acid, whereby ortho- and paranitrophenol, $C_6H_4(NO_2)OH$, are formed. These are separated by distillation with steam, the residuary para- compound being afterward decolorized and crystallized, and treated with sodium hydroxide, forming sodium nitrophenol, $C_6H_4(NO_2)ONa$. By heating this compound with ethyl iodide, paranitrophenetol, $C_6H_4NO_2OC_2H_5$, and sodium iodide are obtained; the former being converted into para-amidophenetol or paraphenetidin, $C_6H_4NH_2OC_2H_5$, by the action of nascent hydrogen obtained from anhydride of orthosulphamidebenzoic acid, and commercially better known as saccharin. The British Pharmacopœia recognizes it under the name Gluside. When toluene is treated with sulphuric acid at 100° C. (212° F.) a mixture of ortho- and paratoluenesulphonic acids, $C_6H_4(CH_3)SO_3H$, is formed, from which the respective calcium salts may be obtained, and then, by mutual decomposition with sodium carbonate, the corresponding sodium salts. From these a mixture of ortho- and paratoluenesulphochlorides, $C_6H_4(CH_3)SO_2Cl$, is obtained by the action of phosphorus pentachloride, and the para-modification caused to crystallize by strong cooling. If dry ammonia gas be allowed to act on orthotoluenesulphochloride, the corresponding sulphamide, $C_6H_4(CH_3)SO_2NH_2$, is formed, which upon oxidation with potassium permanganate yields potassium orthosulphamidebenzoate. The latter salt when decomposed by means of an acid does not yield free orthosulphamidebenzoic acid, but instead the acid splits up into its anhydride and water, the former of which may then be crystallized from alcohol or boiling water.

Benzosulphinide is not very soluble in water, requiring at least 250 parts at 25° C. (77° F.), but is soluble in 25 parts of boiling water or alcohol. Although it has been suggested as a desirable sweetening agent for food in certain diseases, it hardly seems to merit a place in the Pharmacopœia and is not used in any of the official preparations. It is said to have 500 times the sweetening power of sugar and its sweet taste is perceptible even in dilutions of 1 to 10,000. Since parasulphamidebenzoic acid does not possess a sweet taste, its presence would materially reduce the sweetening power of the official article; the British Pharmacopœia recommends a special test for the same by allowing a strong solution to crystallize and then testing the melting-point of the crystals. Crystals of parasulphamidebenzoic acid melt at 280° to 283° C. (536°–541.4° F.), while those of benzosulphinide melt at 218.8° to 220° C. (426°–428° F.).

The solubility of benzosulphinide in water is greatly increased by the presence of alkali carbonates and bicarbonates, orthosulphamidebenzoates being formed. The sodium salt, $C_6H_4COSO_2N.Na + 2H_2O$, is commercially known as *soluble saccharin*, *soluble gluside*, and *crystallose*, and should not be confounded with the official benzosulphinide, which is sometimes designated as insoluble saccharin.

Besides the name saccharin, the following have also been applied to commercial benzosulphinide: *neosaccharin*, *glucusimide*, *benzoylsulphonimide*, etc.

Methylthionine Hydrochloride. Methylene Blue. $C_{16}H_{18}N_3SCl$.—The full chemical name of this compound is tetramethylthionine hydrochloride, but it is better known by its trade-name, methylene blue, which has also been adopted as one of the official English names. It may be prepared by treating a solution of amidodimethylaniline, known also as dimethyldiamidobenzene, $C_6H_4(NH_2)N(CH_3)_2$, in hydrochloric acid with hydrogen sulphide and then with ferric chloride. It occurs both as a dark-green crystalline powder and in form of prismatic crystals having a bronze-like lustre, which dissolve readily in water with deep-blue color. The Pharmacopœia requires that if 2 Gm. of the salt be ignited, not more than 0.008 Gm. of residue shall remain and be free from zinc oxide.

Methylene blue is usually dispensed in capsules, either dry or in form of a mass. Some little care is necessary to avoid soiling the hands and clothing of the operator. When it is ordered in powder form, the best plan would seem to be to rub the methylene blue into powder, not too fine, in a glass mortar, and divide the powder into the prescribed number of doses on glazed paper, and then carefully transfer to the capsules. If a mass is to be made, methylene blue may be rubbed into powder with half its weight of powdered licorice root and then massed with glucose or some similar excipient. By keeping the hands and pill-tile well dusted with licorice powder, it is possible to prevent coloring while the mass is divided into the required number of cylinders, which may then be transferred to the capsules in the usual manner with the aid of a long needle.

Commercially, methylene blue is sometimes found as the double chloride of zinc and tetramethylthionine, in which form it is used as a dye, but is unfit for medicinal purposes, hence the test for absence of zinc, given above. It must not be confounded with methyl blue, which is made by treating pararosaniline with aniline and the resulting product with sulphuric acid. A solution of methyl blue, upon the addition of sodium hydroxide, changes to reddish-brown, whereas the color of methylene blue solution changes to violet.

CHAPTER LV.

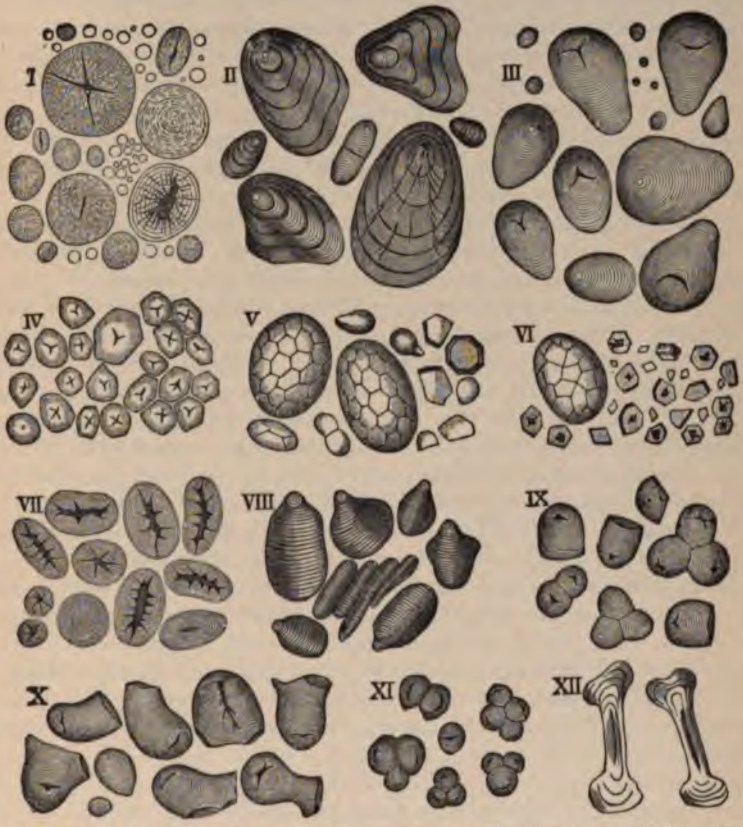
STARCHES, GUMS, AND SUGARS.

BESIDES cellulose, certain other principles are widely diffused in the vegetable kingdom, which are of more or less interest to pharmacists, either as useful medicinal agents or because they must be excluded in the preparation of certain galenicals. These are known as amylaceous, mucilaginous, and saccharine principles, and are usually designated as starches, gums, and sugars. The investigations of E. Fisher and others regarding the chemical character of these well-known plant-products have so completely changed the views formerly entertained, and so enriched the knowledge regarding their intimate relationship, that chemists now consider starch, gum, and sugar, and also cellulose, as members of a group designated as saccharides; in regard to their chemical character, they are looked upon as aldehydes, ketones, and ether-like anhydrides derived from certain hexatomic alcohols.

Starch.—This substance occurs chiefly in the seeds, roots, and rhizomes of plants, where it appears deposited for the purpose of future nourishment either of the germinating embryo or during the next year's growth of the plant itself. When viewed with the naked eye, starch appears as a structureless substance in the form of a powder, but under the microscope it is seen to consist of round, ovate, lenticular, or polyhedral granules or cells, differing in size and shape according to the source whence the starch has been taken, as may be seen in Fig. 297. Starch granules appear to consist of concentric layers of varying density, arranged around a nucleus or hilum situated in the centre of the granule, or more generally at one end or near the margin. The formation of starchy matter and the manner of its deposit belong more properly to the study of physiological botany.

While a valuable dietetic and article of food, starch possesses little or no medicinal virtue, and, as its presence largely interferes with the stability of pharmaceutical preparations, it is sought to be excluded by the use of appropriate menstrua. Starch is insoluble in cold water, strong or diluted alcohol, and ether, but when treated with boiling water solution takes place, and a more or less gelatinous mucilage results upon cooling. This peculiar behavior with water is due to the fact that the starch granules have a very hard outer coating (by some authorities looked upon as a distinct membrane), to which the name farinose or amylin has been given; this is ruptured by the boiling water, after which the white contents of the granule, known as granulose or amidin, are dissolved. Prolonged trituration of starch with sand causes a similar rupture of the farinose, when a portion of the amidin will also be taken up by cold water. Complete solution of the granules does not occur even with boiling water, as the farinose remains undissolved, but it can be rendered soluble by the action of sulphuric acid. If starch paste, made by mixing starch with water heated to 75° C. (158° F.), be boiled for some time, it is gradually converted into a clear liquid capable of being filtered, and if this liquid be added to a large volume of alcohol, a water-soluble modification, known as amylogen, is precipitated in the form of a white powder; this amylogen may be

Fig. 297.



I, Wheat starch. II, Potato starch. III, Arrowroot or Maranta starch. IV, Corn starch. V, Oat starch. VI, Rice starch. VII, Bean starch. VIII, Curcuma starch. IX, Tapioca starch. X, Sago starch. XI, Sarsaparilla starch. XII, Euphorbia starch.

preserved under alcohol, and as long as it is not dried will remain soluble in cold water. Amylogen is likewise produced if starch be mixed with 16 or 18 times its weight of glycerin and then kept at a temperature of 190° C. (374° F.) for about a half hour, the resulting clear liquid being then precipitated as above stated. Saturated solutions of calcium chloride and potassium iodide effect the same change without the aid of heat.

In composition starch is isomeric with cellulose, but differs from it in physical and many chemical properties. The most delicate reagent for starch is iodine, which strikes a characteristic blue color with cold solutions of starch, and in the form of solution is used to detect starch in vegetable tissues. Conversely, starch mucilage is extensively employed in iodimetry as an indicator; the union between starch and iodine is, however, a very feeble one, and not considered to be of a chemical character, as it is easily broken up by heat.

All air-dried starch when heated at 100° C. (212° F.) to constant weight loses about 14 per cent. of water, which is gradually reabsorbed on exposure to the air; if anhydrous starch be mixed with a small quantity of water, it absorbs the same with evolution of heat, as certain inorganic salts absorb water of crystallization. When heated for some time to 170°–200° C. (338°–392° F.) starch is gradually converted into dextrin and becomes soluble in cold water, losing at the same time its property of being colored blue by iodine. The same result occurs if starch be heated with diluted nitric or sulphuric acid, the change, however, taking place in less time and at a lower temperature; if the action of the diluted acids be allowed to continue for a longer period, the dextrin is finally converted into dextrose (glucose). Diastase, the active ferment of malt, also effects the hydrolysis of starch into dextrin, and finally into a kind of sugar, differing, however, from dextrose, and known as maltose; for this reason starch paste is used in the valuation of malt extracts. The value of proper mastication of bread and other starchy food depends upon a thorough admixture with saliva, which contains a ferment, known as ptyalin, having the same effect on starch as diastase.

Dextrin is extensively made for the market from potato starch, either by the dry-heat process above mentioned or by mixing the starch into a paste with water acidulated with nitric acid, pressing the paste into cakes, drying, powdering, and heating for one or two hours at 110° C. (230° F.). Dextrin occurs in two varieties, white and yellow, which are soluble in cold as well as hot water, forming a mucilaginous liquid; it has a sweetish taste, peculiar odor, and is known also as British gum. Iodine colors dextrin pink or reddish, unless unaltered starch is present, when a purplish tint results.

Two substances, allied to starch and isomeric with it in composition are met with in certain drugs; these are lichenin and inulin, the former occurring in cetraria and the latter in inula, taraxacum, etc. *Lichenin*, known also as moss-starch, is obtainable from Iceland moss and other lichens; it is soluble in boiling water and gelatinizes upon cooling; iodine imparts to it a yellow or brown color. *Inulin*, found in place of starch in the roots and underground stems of many Compositæ, forms a clear solution with boiling water and does not gelatinize upon cooling; continued boiling with water converts it into a sugar, known as fructose. It is colored yellow by iodine and does not occur in the form of concentric layers, nor does it contain a definite and constant proportion of water like starch.

Starch is obtained for use by washing it out with water from the material containing it, the mixture being transferred to large sieves or straining-bags, which allow the starch to pass through with the water and retain the cellular fibre. In the case of potatoes, these are first grated, while wheat, corn, etc., are treated in the form of flour. Since cereals contain a nitrogenized principle or ferment, called gluten, intimately mixed with the starch, this is removed either by means of incipient fermentation not affecting the starch, or it may be separated by kneading the flour in muslin bags while a stream of water continually falling on it washes out the starch, leaving the gluten behind. The different varieties of starch can best be distinguished from each other by their shape and size under the microscope, but some show also differences in their behavior with hot water and also hydrochloric acid.

Official starch, recognized in the Pharmacopœia by the general Latin term *amylum*, is corn starch, and is used in preparing the official glycerite of starch. Starch was known to the ancients, who applied the name amylum (derived from the Greek μύλος, a millstone, and the prefix ἀ, meaning privative or without) to the substance, because starch could be obtained without grinding between stones, as in the case of flour.

Gums.—These are amorphous translucent substances, in all probability excretory products, obtained usually as exudations. They differ from starch in being wholly or partly soluble in cold water and in not being colored blue by iodine; the blue coloration produced in tragacanth is due solely to the presence of starch. Gums may be divided into two classes, which differ from each other in physical as well as chemical properties; for convenience they are known as gums and mucilages, respectively. As stated on pages 201 and 326, gums are precipitated from their aqueous solution by strong alcohol and solutions of ferric chloride and sodium borate and silicate, the precipitate in the last three cases being of a gelatinous character. Diluted alcohol, containing less than 60 per cent. by volume of absolute alcohol, is capable of dissolving gums (the quantity taken up increasing with the decreasing proportion of alcohol present), but glycerin has no solvent effect whatever, although it mixes clear with aqueous solutions of gums. The most delicate as grape-sugar or starch-sugar. In nature dextrose is found associated with fructose or fruit-sugar in numerous fruits and in honey; it occurs also in certain secretions of the human body as the result of a disease known as diabetes mellitus. Artificially, it is manufactured on a large scale from corn starch by treatment with diluted sulphuric acid, the process being conducted in both open and closed converters, of which the latter require the application of a higher heat, but a shorter time, to complete the change. As stated on page 632, the first action of the diluted acid is to change the starch into dextrin, which is finally converted into dextrose; liquid or syrupy glucose usually contains unconverted dextrin, while in the solid grape-sugar the complete conversion into dextrose has been carried out. Corn-starch is always mixed with gluten, which is removed by treatment with sodium hydroxide, after which the starch is mixed with water to a creamy consistence and run into the diluted acid and heated by means of steam until all starch has been converted; the acid is then neutralized by means of calcium carbonate and the liquid filtered, passed through animal charcoal, and concentrated. Commercial glucose is rarely pure, being frequently of acid reaction or containing sulphates and chlorides. Liquid glucose, also known as corn-syrup, is a colorless or light yellowish, sweetish syrup, of 1.40 to 1.43 specific gravity, and contains from 40 to 50 per cent. of dextrose, and from 30 to 40 per cent. of dextrin. Calcium sulphite, added as a preservative, is found in nearly all commercial glucose, and to its presence is to be ascribed the decolorizing action of the latter on solutions containing iodine in a free state.

Grape-sugar separates as a granular crystalline deposit in honey, and can be obtained in a hydrated form, $C_6H_{12}O_6 + H_2O$, in small, wart-like crystals from its aqueous or hydro-alcoholic solution; from a hot solution in alcohol or methyl alcohol it separates in anhydrous prismatic crystals. It is soluble in very nearly its own weight of water and in 50 parts of alcohol at 15° C. (59° F.), the solutions possessing a far less sweet taste than those of ordinary sugar. At 60° C. (140° F.) grape-sugar softens, and at 86° C. (186.8° F.) melts completely.

Dextrose is directly fermentable, its solutions are not affected by strong sulphuric acid, but when heated with alkali hydroxides acquire a dark color; upon addition of ammoniacal solution of lead acetate dextrose is precipitated from its solution, but is not affected by neutral or basic lead acetate.

Various tests can be used for the detection of dextrose, such as Trommer's test (cupric sulphate, solution of potassium hydroxide, and heat), causing a deposit of brick-red cuprous oxide; Moore's test (solution of potassium hydroxide and heat), causing a dark, almost black, color; Boettger's test (bismuth subnitrate, solution of potassium hydroxide and heat), causing a black precipitate of metallic bismuth, and others. For the quantitative determination of dextrose, volumetric alkaline solution of cupric tartrate, known as Fehling's Solution, is usually employed; each Cc. of this solution corresponds to 0.005 Gm. of anhydrous dextrose. When Fehling's Solution is boiled in the presence of dextrose, yellowish hydrated cuprous oxide is first formed, which is finally changed into the anhydrous brick-red variety. Since dextrin also reduces the cupric salt of Fehling's Solution, its absence must first be ascertained in all quantitative determinations by this method. Barfoed's Solution, consisting of 13.3 Gm. of crystallized cupric acetate and 2 Gm. of glacial acetic acid in 200 Cc. of water, suffers reduction with all glucoses, but not with dextrin.

The name dextrose was given to this particular sugar on account of its dextro-rotatory power, since it invariably deflects the ray of polarized light to the right when examined by means of a polariscope. An explanation of the uses of the polariscope can be found on pages 580 and 581 of the Pharmacopœia.

The British Pharmacopœia recognizes an official syrup of glucose, made by mixing commercial liquid glucose with twice its weight of syrup.

Fructose, or **levulose,** is of interest chiefly as a natural constituent of honey; it occurs also associated with dextrose in many fruits, and is therefore known as fruit-sugar. The name levulose was given it because it is lævo-rotatory—that is, causes the plane of polarized light to deviate to the left. When pure, it occurs as a colorless or faintly yellowish syrup of very sweet taste, which crystallizes with great difficulty; it remains in the liquid portion of honey after all the granular dextrose has been removed. As stated under Starch, fructose is formed also by prolonged boiling of inulin with diluted acids. The term inverted sugar is usually applied to the mixture of dextrose and fructose, whether obtained by inversion of cane-sugar by means of diluted acids and heat, or by some special ferment, such as that supplied by bees in the manufacture of honey.

Natural honey contains from 65 to 80 per cent. of a mixture of dextrose and levulose, together with small portions of cane-sugar, besides 20 or 30 per cent. of water and about 0.1 per cent. of formic acid. During the clarification of honey the acid is generally dissipated, and possibly on this account clarified honey is more prone to fermentation than the crude article. Commercial honey is frequently adulterated with a solution of glucose and dextrin; the latter can be detected by addition of an excess of official alcohol to an aqueous solution of honey. Any dextrin present will be precipitated in the form of white flocculi.

Polysaccharides appear to be the result of condensation of two or more molecules of one or any two members of the group of glucoses, water being eliminated at the same time; hence they may be considered as ether-like anhydrides; thus, $2C_6H_{12}O_6 = C_{12}H_{22}O_{11} + H_2O$. In support of this view, the members of this group have been found to take up water and split up into equal molecules of glucoses if heated with diluted acids. These sugars are darkened and is said to exist also in the fruit of Achras sapota, a tree of the West Indies, this being the only known case of its occurrence in the vegetable kingdom. Milk-sugar is obtained by crystallization from the whey or thin fluid remaining after removal of the casein or albuminous principle by coagulation. The crude granular product is purified by resolution, filtration, and recrystallization. Prior to 1890 the world's supply of milk-sugar was furnished by Europe, chiefly Switzerland, but since then large quantities are being manufactured in this country, the present annual production being estimated at about 1,500,000 pounds.

The crystals of sugar of milk contain 5 per cent. of water, which is not lost until a temperature of 130° C. (266° F.) is reached. They are very hard, and require about 6 or 7 parts of water for solution, the solution being far less dense than one of either dextrose or cane-sugar of equal concentration, and far less sweet in taste. As found in the shops, sugar of milk is always in the form of powder, which feels gritty between the teeth. In pharmacy it is used exclusively as a diluent in the preparation of triturations, powdered extracts, etc., for which purpose it is admirably adapted, as it is non-hygroscopic.

Like dextrose, sugar of milk is dextro-rotatory, and also reduces an alkaline solution of cupric tartrate, but does not reduce Barfoed's Solution of cupric acetate (see page 637). Boiled with diluted acids, sugar of milk yields dextrose and galactose; the latter crystallizes in large prisms and yields mucic acid, insoluble in cold water when treated with nitric acid, whereas dextrose yields saccharic acid, which is soluble.

The presence of cane-sugar in sugar of milk may be recognized, as stated in the Pharmacopœia, by sprinkling about 1 Gm. of the suspected sugar upon 5 Cc. of sulphuric acid, contained in a flat-bottomed dish, and then covering with a watch-glass to prevent the admixture of dust and other matter; the acid should acquire at most a greenish or reddish, but no brown or brownish-black, color within half an hour. It is important that no heat be applied during this test, as milk-sugar itself will char at an elevated temperature in the presence of the acid.

Maltose, or malt-sugar, is produced by the action of diastase of malt on starch, either during the germination of the barley or when diastase is mixed with starch and water and kept at a temperature of 70° C. (158° F.). It is directly fermentable, and is of considerable interest in pharmacy on account of the part it plays in the fermentation of grain in the manufacture of alcohol. When hydrolyzed by means of diluted acid or by the action of diastase or yeast, maltose splits up into two molecules of dextrose. Maltose crystallizes with one molecule of water, and is readily soluble in water; although strongly dextro-rotatory, it can be distinguished from dextrose, like milk-sugar, by means of Barfoed's Solution.

CHAPTER LVI.

ALCOHOL AND ITS DERIVATIVES.

ALTHOUGH, in chemistry, the term alcohol is used to designate a group of compounds derived from hydrocarbons of the methane or fatty series, by replacement of one or more hydrogen atoms by a corresponding number of hydroxyl groups, which have certain chemical properties in common, it is restricted in pharmacy to one substance, chemically known as ethyl alcohol, and recognized in the Pharmacopœia also by the simple term alcohol. When other alcohols are used in pharmacy they are either designated by specific names, such as glycerin, mannitol, etc., or, by adding a qualifying prefix to the word alcohol, as amyl alcohol, methyl or wood alcohol, etc., to distinguish them from ordinary or ethyl alcohol.

Alcohol is obtained in this country almost exclusively from grain, while in Europe potatoes are extensively employed, by a process known as vinous fermentation. Fermentation is a process of decomposition differing from putrefaction in that the resulting products are, as a rule, valuable, or at least useful, and not accompanied by offensive gases; fermentation is usually applied to the decomposition of substances composed of carbon, hydrogen, and oxygen; while if nitrogen and sulphur are also present the term putrefaction is more aptly used, on account of the putrid or foul odor emitted by such bodies during decomposition. Certain conditions are essential to both processes of decomposition, namely, the presence of air, moisture, heat, and certain agents known as ferments. There are fermentations of various kinds, such as saccharine, vinous, mucic, lactic, butyric, and acetous, depending upon the chemical constitution of the substances undergoing change, some of these being in reality oxidation-processes not due to fermentative action.

The first step necessary in the manufacture of alcohol is the saccharine fermentation, known also as the mashing process, which consists in the conversion of starch into sugar by means of diastase. This latter substance is produced during the germination of grain, as in the malting of barley. **Malt** is made by well moistening barley with water and spreading it, about two feet deep, on stone floors, in dark rooms; heat is developed, and partial germination is allowed to go on, during which time *diastase* is produced, the barley assuming a darker color and peculiar odor, while the starch of the grain is converted into dextrin and malt-sugar. Diastase is capable of converting 2000 times its weight of starch into maltose. When isolated, it is a white tasteless solid, soluble in water and weak alcohol, but precipitated by strong alcohol, and rendered inert by the heat of boiling water.

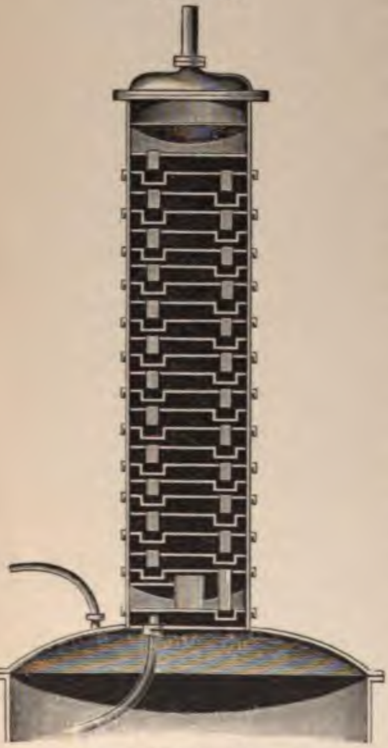
During the mashing process large quantities of raw grain are kept in contact with malt and water at a moderately elevated temperature, whereby the starch by action of the diastase is first changed to malto-dextrin and maltose, and finally all converted into dextrose, apparently by the simple appropriation of water, as shown by the following equations :

$$(1)\quad \underset{\text{Starch.}}{4C_6H_{10}O_5} + 2H_2O = \underset{\text{Maltose.}}{2C_{12}H_{22}O_{11}}$$

$$(2)\quad \underset{\text{Maltose.}}{C_{12}H_{22}O_{11}} + H_2O = \underset{\text{Dextrose.}}{2C_6H_{12}O_6}$$

The saccharine solution thus obtained is known as wort, and, after addition of some yeast, is allowed to undergo fermentation at a temperature which is maintained between 15° and 30° C. (59° and 86° F.), whereby a weak alcoholic liquid is produced, due to the splitting up of dextrose into alcohol and carbon dioxide: thus, $C_6H_{12}O_6 = 2C_2H_5OH + 2CO_2$. Besides alcohol and carbon dioxide, however, some amyl alcohol and other homologous products, collectively designated as fusel oil, are also produced, and Pasteur has shown that small quantities of glycerin (3 per cent.) and succinic acid (0.6 per cent.) are invariably formed. The composition of these so-called low wines, or weak spirits, varies with the starchy material used in their manufacture; thus, potato starch always yields a much larger proportion of amyl alcohol than grain starch, while grain spirit is contaminated with œnanthic and other ethers. The percentage of alcohol in mashed and fermenting mixtures never exceeds 14 per cent., since the yeast plant cannot live in fluid containing a larger percentage.

FIG. 298.



Column still or dephlegmator.

Distillation of the fermented liquid furnishes a product much richer in alcohol (raw whiskey), which is then further rectified by treatment with recently burned charcoal and subsequent distillation in stills provided with a series of condensers, in the first of which much of the water and amyl alcohol is retained, allowing a purer and stronger alcohol to pass on to the other condensers. For the further removal of water and foreign odors from alcohol, distillation over sodium manganate, anhydrous sodium acetate, and freshly burned lime is employed.

For the purpose of facilitating the rectification of alcohol on a large scale, use is made of a distilling column or dephlegmator, which is interposed between the still proper and the condenser, and, as shown in Fig. 298, consists of a series of communicating chambers, one above the other. The vapor rising from the still enters the lowest chamber through a narrow tube projecting upward into the chamber, and, having filled the space, passes into the next compartment through a second tube situated on the opposite side to that through which the vapor entered. By this arrangement the less volatile vapors will be condensed, and the resulting fluid collects on the bottom of each compartment, and if in sufficient quantity to rise above the projecting tube it flows into the next lower chamber, thus gradually separating the less volatile vapors from the more volatile, and finally allowing only the more volatile vapor to pass from the uppermost compartment into the condenser. Naturally the continual influx of hot vapor from the still keeps the liquid collecting on the bottom of the several compartments warmed, whereby the more volatile portions are constantly being vaporized and loss thus avoided.

During the past ten or fifteen years alcohol has been successfully produced from cellulose by treating dried peat with very dilute sulphuric acid for several hours at a temperature of 120° C. (248° F.), whereby peat-sugar is formed, which is subsequently fermented with yeast and distilled, yielding as much as 62 liters of absolute alcohol for 1000 kilogrammes of dry peat used (about 15 gallons for each ton).

The Pharmacopœia recognizes three different grades of strength of alcohol, designated by specific names, thus :

		Percentage of True Ethyl Alcohol.	
		By weight.	By volume.
Alcohol	about	92.3	94.9
Absolute alcohol		99.0	99.5
Diluted alcohol	about	41.5	48.9

Whenever alcohol and water are mixed, heat is evolved and contraction of volume results, both varying with the proportions of the liquids used. According to Flückiger, the rise of temperature will be greatest when 30 parts by weight of absolute alcohol are mixed with 70 parts by weight of water, amounting to 9 degrees C., or 16.2 degrees F., and the greatest contraction occurs when 58 volumes of absolute alcohol are mixed with 54 volumes of water, amounting to a loss of 4 volumes or 3.57 per cent. of the total mixture.

The use of the alcoholometer for ascertaining the percentage strength of commercial alcohol has been fully explained on page 64, and rules have been given on page 73 for preparing weaker alcohol from a stronger variety by dilution with water. Besides, the Pharmacopœia gives specific directions, under Diluted Alcohol, for preparing mixtures of definite strength.

Commercial alcohol does not always come up to the requirements of the Pharmacopœia for official alcohol, averaging, as a rule, from 91 to 93 per cent. by volume of ethyl hydroxide; but the variety sold as *Cologne spirit* generally contains 94.5 or 95 per cent.; the latter is also to be preferred on account of its freedom from foreign odor. Alcohol which has been stored for some time in barrels, particularly if the latter have been imperfectly charred on the inside is apt to be contaminated with coloring-matter and tannin. As found on the market, ordinary alcohol, and even Cologne spirit, frequently has an acid reaction, due to the presence of acetic acid, derived from the aldehyde always more or less present. It is therefore necessary to redistil such alcohol from potassium hydroxide or lime before using it for analytical purposes, especially the titration of alkaloids.

Since alcohol may be adulterated with methyl alcohol, the Pharmacopœia gives a special test for detection of the latter, as follows, by which the presence of as little as 2½ per cent. may be determined: Into a test-tube, of the capacity of about 40 Cc., 1 Cc. of the alcohol or spirit to be tested should be poured, and, if it be undiluted, enough distilled water added to make 10 Cc. in all. If the alcohol be already diluted, a correspondingly larger measure of it is taken and diluted to 10 Cc., so that the proportion of the alcohol in the liquid shall not be more than about 10 per cent. by volume. A copper wire spiral (made by winding a piece of No. 18 clean copper wire 1 meter long closely around a glass rod 7 millimeters thick, making a coil about 3 centimeters long, the end of the wire being formed into a handle) should be heated to redness in a flame free from soot, then plunged steadily quite to the bottom of the liquid in the test-tube and held there for a second or two, then withdrawn and dipped into water to cool. This treatment with red-hot copper should be repeated five or six times, immersing the test-tube in cold water to keep down the temperature of the liquid. The contents of the test-tube are now filtered into a wide test-tube and boiled very gently. If the odor of acetaldehyde be perceptible, the boiling is to be continued until the odor ceases to be distinguished clearly. The liquid is now cooled, and to it is added 1 drop of a solution containing 1 part of resorcinol in 200 parts of water. A portion of this liquid is then poured cautiously into a second tube containing pure sulphuric acid, the tube being held in an inclined position, in such a way that the two liquids shall not mix; this tube is allowed to stand for three minutes, and then slowly rotated. No rose-red ring should show at the line of contact of the two layers. The test depends on the formation of formaldehyde from methyl alcohol by the oxidizing effect of the red-hot copper, and the reaction between this and resorcinol, as shown by the rose-red color.

Absolute Alcohol is intended to be identical with official alcohol as far as the absence of amyl alcohol and other impurities is concerned, but contains far less water than the latter, the Pharmacopœia not allowing more than 1 per cent. by weight. The entire absence of traces of moisture is practically impossible, although the amount is reduced to less than 0.5 per cent. by some manufacturers. Among the various dehydrating agents suggested, freshly burned lime has been found most desirable.

In the manufacture of absolute alcohol, high grade commercial alcohol (95 per cent.) free from foreign odor, is either shaken with the lime in coarse powder for some time, or caused to percolate repeatedly through alternate layers of fine and coarse granules of lime, in an apparatus so arranged as to avoid all contact with air, after which it is transferred, without exposure, to a column-still and distilled at a low temperature, under reduced pressure, by which means the alcohol vapor is made to pass through several condensing chambers, in which any aqueous moisture still remaining will be separated and flow back into the still.

Absolute alcohol is very hygroscopic, and should be preserved in tightly stoppered bottles containing either some anhydrous cupric sulphate or pieces of freshly burned lime. In pharmacy its use is confined to that of a solvent for phosphorus and similar substances, but in the manufacture of certain chemicals it is more extensively employed.

Diluted Alcohol, a most valuable solvent for many vegetable principles, is made by mixing equal volumes of official alcohol and water. Since the mixture suffers nearly 3 per cent. loss by contraction, the finished, cooled product contains about 48.9 per cent. by volume of absolute ethyl alcohol. It should not be used until the temperature of the mixed liquids has fallen to that of the room.

Proof spirit, as recognized by the U. S. Government, contains 50 per cent. by volume of absolute alcohol, and is reckoned by gaugers as equivalent to 100 degrees; hence, the terms 25 or 40 above or below proof do not refer to liquids containing 25 or 40 per cent. of alcohol, more or less, than the 50 per cent. proof spirit, but only one-half as much, namely, 12.5 or 20 per cent., each proof degree representing 0.5 per cent. of absolute ethyl alcohol. Official 94.9 per cent. alcohol is thus said to stand at 189.8 degrees, or 89.8 degrees above proof.

Derivatives of Alcohol.—The following preparations made from ethyl alcohol are officially recognized in the Pharmacopœia, and therefore of special interest to pharmacists: ether, acetic ether, ethereal oil, ethyl carbamate, ethyl chloride, spirit of nitrous ether, paraldehyde, chloroform, hydrated chloral, and iodoform. In addition, a few allied and some unofficial preparations will also be considered.

Ether.—The general term ether is used by chemists to designate oxides of hydrocarbon radicals; both simple and mixed ethers are known, as the oxygen may be united to two groups of the same or mixed radicals; thus, $(C_2H_5)_2O$, ethyl ether, and $(CH_3)_2O$, methyl ether, are simple ethers, while $(CH_3C_2H_5)O$, methyl ethyl ether, is a mixed ether.

The Pharmacopœia recognizes but one compound by the name ether (Latin *æther*), namely, ethyl ether or ethyl oxide, $(C_2H_5)_2O$, and in all official formulas and physicians' prescriptions this substance is to be understood as intended. Ethyl ether is sometimes called sulphuric ether, and several commercial varieties, known as concentrated and washed ether, are found on the market; but as their strength and purity are not stated on the label, they should not be used in place of the official ether. The process of ether manufacture consists in heating a mixture of alcohol and sulphuric acid in a suitable still, by means of steam coils, to 130° C. (266° F.), and, when the distillation of ether begins, allowing a continuous supply of alcohol to fall into the still from a feed-back so regulated that the mixture shall be kept at a constant quantity and temperature. The vapors are passed through two purifiers: the first one, of cast-iron, containing a solution of potassium hydroxide, in which water and other impurities are washed out; the second one, of block tin, is provided with a bed of pebblestones, where alcoholic and other vapors having a higher boiling-point than ether are recondensed and carried to the feed-back near the still. In order that no ether may be lost, both purifiers are kept heated, the purified ether vapor being finally condensed in a large worm surrounded by running water.

Etherification may thus be explained: when alcohol and sulphuric acid are mixed, one molecule of each combines to form ethylsulphuric acid and water, $C_2H_5OH + H_2SO_4 = C_2H_5HSO_4 + H_2O$. In the presence of heat and an excess of alcohol a further reaction ensues, ether being produced and sulphuric acid regenerated; thus, $C_2H_5HSO_4 + C_2H_5OH = (C_2H_5)_2O + H_2SO_4$.

The theoretical yield of ether amounts to nearly 5 pounds for each gallon of alcohol used, but in practice rarely more than 4 pounds are recovered. It is important that the temperature be kept between 130° and 138° C. (266° and 280.4° F.), so as to avoid the distillation of much alcohol vapor and the formation of other compounds. Since sulphuric acid is continually regenerated its power of etherifying alcohol is theoretically without limit, but in practice it is found that water and other impurities in the alcohol gradually interfere, the acid being diluted and becoming black while the mixture in the still begins to froth. According to the late Dr. Squibb, a charge of 360 pounds of concentrated sulphuric acid is sufficient for the etherification of 120 barrels of good, clean alcohol.

Official ether has a specific gravity of 0.716 to 0.717 at 25° C. (77° F.) and contains 96 per cent. of absolute ethyl oxide; the remaining 4 per cent. consists of alcohol and traces of water which it is impracticable to remove. It is best preserved in tin containers holding from 100 Gm. upward, as they are less liable to breakage than glass. Ether is very inflammable, and its vapor, which is about two and a half times as heavy as air, when mixed with the latter explodes in contact with flame; hence care is necessary in handling and dispensing ether, especially at night.

Besides being used in various manufacturing processes, ether enters also into the composition of two alcoholic solutions, designated in the Pharmacopœia as spirit of ether and compound spirit of ether (see page 260), which should be prepared by the pharmacist himself, on account of the variable quality of the commercial articles.

Acetic Ether.—Under this name the Pharmacopœia recognizes a somewhat impure ethyl acetate, $C_2H_5C_2H_3O_2$ or $CH_3COOC_2H_5$, the impurities being chiefly alcohol and water. Much of the acetic ether found on the market is of inferior quality, and, as its manufacture presents no difficulties, the following process of Hager is recommended, the author having repeatedly used it with much satisfaction: 126 Gm. of official alcohol are mixed with 218 Gm. of 94 per cent. or 222 Gm. of official (92.5 per cent.) sulphuric acid, and the mixture allowed to stand for two or three days in a well-closed flask, so that ethylsulphuric acid may form. Having rendered a quantity of sodium acetate anhydrous, by heating at 130° C. (266° F.) to constant weight, 164 Gm. of this acetate, in powder, are placed in a retort and the acid-alcohol mixture carefully added. The retort is heated in a water-bath and the vapors condensed in a well-cooled receiver as long as a brisk reaction continues; the final distillate is collected separately, as it is likely to be contaminated more largely with acetic acid. The reactions occurring in the foregoing process, may be illustrated by the equations $C_2H_5OH + H_2SO_4 = C_2H_5HSO_4 + H_2O$ and $C_2H_5HSO_4 + NaC_2H_3O_2 = C_2H_5C_2H_3O_2 + NaHSO_4$.

Crude acetic ether is always more or less contaminated with alcohol and acetic acid, which are removed by repeatedly agitating the ether with one-third of its volume of a 20 per cent. sodium chloride solution containing also 2 per cent. of sodium carbonate and carefully decanting the ethereal layer. Milk of lime and caustic alkalies should not be used, since the acetic ether would thereby be decomposed and converted into alcohol and the respective acetate. For the removal of water, the purified ether is well shaken for some time with freshly ignited potassium carbonate and redistilled in a water-bath; dehydrated acetic ether is far more stable than that containing water.

Official acetic ether should be neutral to litmus-paper, contain not less than 90 per cent. of ethyl acetate, and be soluble in not less than 7 parts of water at 25° C. (77° F.); absolute ethyl acetate requires about 16.5 parts of water for solution.

Ethereal Oil.—This name is applied in the Pharmacopœia to a volatile liquid composed of equal volumes of so-called heavy oil of wine and ether. Heavy oil of wine is a somewhat complex mixture, containing from 44 to 48 per cent. of esters, chiefly diethyl sulphate, $(C_2H_5)_2SO_4$, besides other compounds regarding which no satisfactory information exists. The official directions for preparing heavy oil of wine are to distil a mixture of equal volumes of alcohol and sulphuric acid (previously allowed to stand for twenty-four hours, partly to separate lead sulphate), on a sand-bath, at a temperature between 150° and 160° C. (302° and 320° F.), as long as oily drops pass over. The ethereal liquid is separated from the distillate and exposed to the air to free it from ether, after which it is drained on a well-wetted filter and washed with cold water. Pure heavy oil of wine is a yellowish, somewhat thick, oily liquid of a peculiar aromatic odor and having a specific gravity of 1.13 at 15° C. (59° F.). Diluted with an equal volume of ether, it constitutes official ethereal oil, a transparent colorless or pale-yellowish liquid, of 0.905 specific gravity at 25° C. (77° F.).

Ethereal oil is used solely in the preparation of the official compound spirit of ether, in which it is present to the extent of 2.5 per cent. by volume (see page 260).

Much confusion exists regarding the so-called ethereal oil and heavy oil of wine of different manufactures, and some care is necessary in the purchase of the commercial article. It is more than probable that much of the ethereal oil sold, and also of the heavy oil of wine, is a by-product in the manufacture of ether and of entirely different composition from the product obtained by the official process. As the yield of heavy oil of wine does not average over 1 or 1.5 per cent. of the weight of alcohol used, it stands to reason that careful producers cannot furnish true ethereal oil at low figures.

Ethyl Bromide. C_2H_5Br.—This liquid, also known as hydrobromic ether, belongs to the class of compounds called by chemists haloid ethers, the hydroxyl groups in the corresponding alcohols having been replaced by one of the haloid elements. While not official in the United States and British Pharmacopœias, it is recognized in the German Pharmacopœia as *æther bromatus*, and is prepared by distilling a mixture of potassium bromide, alcohol, and sulphuric acid, washing the distillate with potassium carbonate solution and then water, and finally rectifying over calcium chloride. The following equation explains its formation: $C_2H_5OH + KBr + H_2SO_4 = C_2H_5Br + KHSO_4 + H_2O$. Ethyl bromide is a colorless liquid of nearly the same specific gravity as chloroform, but boiling at 38° or 40° C. (100.4° or 104° F.); it has a neutral reaction, but is readily decomposed by light and air, becoming acid and dark in color. It must not be confounded with *ethylene bromide*, $C_2H_4Br_2$, a liquid of 2.163 specific gravity and boiling at 131° C. (267.8° F.).

Ethyl Carbamate. $C_3H_7NO_2$ or $CO.NH_2.OC_2H_5$.—This compound, also known as ethyl-urethane, and commercially usually designated simply as urethane, is an ester of carbamic acid, obtained by the action of alcohol on urea or one of its salts.

In chemistry the general term "urethane" is applied to all ethers of carbamic acid, which acid, however, has thus far never been isolated, and is only known in combination: its most familiar compound is ammonium carbamate, $NH_4NH_2CO_2$, one of the constituents of official ammonium carbonate. If the formula for carbamic acid is assumed to be HNH_2CO_2, then the formation of all urethanes may be explained by the substitution of a univalent radical for the one atom of displaceable hydrogen, which may be brought about in various ways.

Ethyl carbamate may be prepared by allowing an excess of alcohol to react with urea nitrate at a temperature of about 125° C. (257° F.) in a sealed tube for several hours. The resulting mass, when cool, becomes crystalline, and is then dissolved in just sufficient water, the solution being subsequently repeatedly shaken out with ether. After recovery of the ether the residue is distilled and recrystallized from water. The reaction involved is shown by the following equation: $(NH_2)_2COHNO_3 + C_2H_5OH = CO.NH_2.OC_2H_5 + NH_4NO_3$.

Ethyl carbamate occurs in colorless, columnar, odorless crystals, which are soluble in less than their own weight of water or of alcohol at ordinary temperature. It is used as a hypnotic.

Several similar compounds have been introduced under specific names, thus: *euphorin*, which is also known as phenyl-urethane, $CO(NHC_6H_5)(OC_2H_5)$, a crystalline powder, sparingly soluble in cold water; *neurodin*, also known as acetyloxyphenyl-urethane, $C_6H_4(CO_2CH_3)NH.CO_2C_2H_5$, colorless crystals sparingly soluble in cold water; *thermodin*, also known as acetylethoxyphenyl-urethane, $C_6H_4(OC_2H_5)N(COCH_3)(CO_2C_2H_5)$, colorless needle-shaped crystals, very sparingly soluble in cold water.

Ethyl Chloride. C_2H_5Cl.—A haloid derivative of alcohol, also known as hydrochloric ether. It may be obtained by passing dry hydrochloric acid gas into cold absolute alcohol, distilling at a very moderate heat, washing the distillate with water and a weak alkaline solution, and rectifying. It is said also to be made on a large scale by heating a mixture of alcohol and concentrated hydrochloric acid for some time under increased pressure (40 atmospheres) at a temperature of 150° C. (302° F.), and then distilling the resulting product. The ethyl chloride vapors are passed through water warmed to 25° C. (77° F.), then dried by passing over calcium chloride, and finally condensed in well-cooled vessels. The reaction between alcohol and hydrochloric acid is shown by the following equation: $C_2H_5OH + HCl = C_2H_5Cl + H_2O$.

Ethyl chloride is a colorless, mobile, very volatile liquid, having a rather agreeable odor. It has a specific gravity of 0.918 at 8° C. (46.4° F.), and boils at 12.5° to 13° C. (54.5° to 55.4° F.), and hence should be kept in sealed glass tubes in a cool place. As it is very inflammable, it should never be used in proximity to fire. In Europe, more especially in Belgium and France, it is used under the names *chelen* and *kelen*. The Pharmacopœia demands the absence of hydrochloric acid, which can be readily detected by adding a few drops of silver nitrate solution to an alcoholic solution of ethyl chloride, when no turbidity should appear.

Ethyl chloride is usually employed as a local anæsthetic, and recently mixtures of it with other compounds have been introduced for general anæsthesia, such as *anæsthol*, composed of ethyl chloride 17 parts, chloroform 36 parts, and ether 48 parts, all by weight; *somnoform*, composed of ethyl chloride 60 parts, methyl chloride 35 parts, and ethyl bromide 5 parts, all by weight. *Anæsthol* (Speier) is not identical with the preceding, but is a mixture of ethyl chloride and methyl chloride.

Bromoform. $CHBr_3$.—This compound, also known as tribrommethane, belongs to the general group of halogen substitution compounds. It may be obtained by the action of calcium or potassium hypobromite on acetone, the mixture being distilled with the aid of heat. The reaction occurring is shown by the following equation: $C_3H_6O + 3KBrO = C_3H_3Br_3O + 3KOH$; $C_3H_3Br_3O + KOH = CHBr_3 + KC_2H_3O_2$; tribromacetone being formed during the first reaction, and this, reacting with potassium hydroxide, yields bromoform and potassium acetate. The distillate is washed with water, then shaken with sulphuric acid, again washed with water, and finally freed from remaining traces of acid by washing with sodium hydroxide solution; the bromoform thus purified is dehydrated with calcium chloride and carefully distilled, that portion coming over between 148° and 149° C. (298.4°–300.2° F.) being collected.

The official bromoform is a mixture of 99 per cent. of absolute bromoform and 1 per cent. of absolute alcohol, the latter being added as a preservative agent. It is a heavy, colorless, mobile liquid, having an ethereal odor and a sweetish taste resembling chloroform; very slightly soluble in water, but soluble in all proportions in alcohol and in fixed oils. It has a specific gravity of 2.808 at 25° C. (77° F.), and boils at 148° C. (298.4° F.); when cooled to 6° C. (42.8° F.) it solidifies.

Bromoform is unfit for use if it has become colored or if of an acid reaction, showing decomposition; it should be preserved in dark amber-colored bottles in a cool place, and never be exposed to direct sunlight.

Chloroform. $CHCl_3$.—Like bromoform, chloroform belongs to the halogen substitution compounds, and resembles the former preparation in many respects. Formerly all chloroform was made by distilling alcohol with a mixture of chlorinated lime and water, and the British Pharmacopœia still recommends this process, with the addition of slaked lime. The reactions by this method are somewhat complicated, resulting in the final formation of chloroform and calcium chloride and formate. By shaking the distillate with water to remove undecomposed alcohol, crude chloroform is obtained.

Chloroform may also be obtained by treating hydrated chloral with sodium hydroxide, when the following reaction occurs: $CCl_3\text{-}CHO.H_2O + NaOH = CHCl_3 + NaCHO_2 + H_2O$. The chloroform is distilled off, while sodium formate remains in aqueous solution.

Since 1885 nearly all chloroform has been made from acetone by distillation with chlorinated lime, it having been found to be the richest chloroform-yielding substance known. The reaction occurring may be illustrated as follows: $2C_3H_6O + 6CaOCl_2 = 2CHCl_3 + Ca(C_2H_3O_2)_2 + 2Ca(OH)_2 + 3CaCl_2$. The chloroform obtained by this method is quite free from the chlorinated by-products frequently found in that made from alcohol.

For the purpose of purification on a commercial scale, chloroform is made to bubble slowly through two successive deep layers of concentrated sulphuric acid, and afterward brought into intimate contact with anhydrous sodium carbonate for the purpose of removing any water and acid mechanically carried over. Finally, the chloroform is siphoned into a dry still and distilled in a water-bath at a temperature not exceeding 62° C. (142.6° F.). The sulphuric acid destroys any organic impurities present and gradually darkens in color, finally becoming black.

Absolutely pure chloroform is very unstable when exposed to air and diffused daylight; but if air be rigidly excluded, it does not suffer decomposition even in direct sunlight. Experience has proved that the best preservative agent for chloroform is alcohol, and the Pharmacopœia therefore directs the presence of from 0.6 to 1 per cent. of the latter. The chief products of decomposition of chloroform are free chlorine and carbonyl chloride, $COCl_2$, which are readily detected by the official tests, and no chloroform should be used for internal administration which shows any contamination. The present Pharmacopœia recognizes but one kind of chloroform, but the term "purified chloroform" is still used by some manufacturers.

The term formyl terchloride is sometimes applied to chloroform; it may also be called trichlormethane if looked upon as methane or marsh-gas, in which three hydrogen atoms have been replaced by chlorine.

Iodoform. **CHI_3**.—This compound, which is analogous to bromoform and chloroform in chemical composition, is unusually rich in iodine, and may be obtained from alcohol by the action of the former element in the presence of alkali hydroxides or carbonates. It contains about 97 per cent. of iodine. For many years only alcohol was used, and either Bouchardat's or Filhol's process employed. The former consists in heating iodine, potassium bicarbonate, alcohol, and water, in a long-neck flask, to between 60° and 80° C. (140° and 176° F.) until the color has disappeared, then adding small portions of iodine as long as these are taken up and decolorized; the mixture is finally set aside for twenty-four hours and the crystals collected on a filter. About one-third of the iodine is recovered as iodoform, the remainder forming potassium iodide.

Filhol's process insures a much larger yield. Iodine is added in small portions to a warm mixture of sodium carbonate, water, and alcohol, and, after cooling, the crystals are collected; the filtrate is again warmed, some alkali carbonate added, and a rapid current of chlorine passed through the liquid as long as iodoform is separated, which is again collected and the filtrate made to yield more iodoform by repeating the treatment. The formation of iodoform may be illustrated by the following equation: $C_2H_5OH + I_8 + 6KHCO_3 = CHI_3 + 5KI + KCHO_2 + 6CO_2 + 5H_2O$, alkali formate being probably always produced, together perhaps with ethyl iodide, acetic ether, and other compounds. The result appears to be greatly influenced by the relative proportions of the materials used and the temperature employed.

Since 1889 the process of Sulliot and Raynaud has largely been used, by means of which iodoform of unusual purity is obtained. A solution of 50 parts of sodium or potassium iodide (in France, derived from the ash of sea-weed) is mixed with 6 parts of acetone and a solution of 2 parts of sodium hydroxide in 1000 parts of water; a dilute solution of sodium hypochlorite is added drop by drop as long as iodoform is produced, the yield being about the theoretical quantity according to the equation $3NaI + 3NaClO + C_3H_6O = CHI_3 + 3NaCl + NaC_2H_3O_2 + 2NaOH$.

At present considerable quantities of iodoform are made by subjecting a solution of 50 parts of potassium iodide in 300 parts of water and 30 parts of alcohol to electrolysis, while a constant current of carbon dioxide is passed into the liquid.

Iodoform occurs in small, lemon-yellow, scale-like crystals, and also in the form of powder, which have a strong characteristic odor, which to most persons is very disagreeable. It is practically insoluble in water, but dissolves readily in alcohol, ether, and fixed oils. The odor of iodoform in mixtures and ointments may be disguised by the addition to 1 ounce of from 3 to 5 drops of oil of peppermint; Peru balsam, cumarin, the oils of fennel, anise, and others, have also been recommended. The odor adheres persistently to the vessels in which preparations of iodoform have been made, but may be removed by a few drops of oil of turpentine, followed by soap and water.

During the past twenty-five years several substitutes for iodoform have been introduced, but, in spite of the persistent unpleasant odor of the latter, its use by physicians still surpasses that of the proposed substitutes, of which the two best known are iodol and aristol, both of which are recognized in the Pharmacopœia, the latter under the name thymol iodide.

Iodol. C_4I_4NH.—A derivative of pyrrol, also known as tetra-iodopyrrol. It is prepared by the interaction of iodine and pyrrol in alcoholic solution, when, upon the addition of water, iodol is separated in the form of yellow crystalline flocculi. It may also be obtained by adding a solution of pyrrol in sodium hydroxide solution to a solution of iodine and potassium iodide in water, the resulting precipitate being subsequently washed with water. Pyrrol is a basic liquid, lighter than water, obtained by fractional distillation from animal oil after purification of the latter; its composition is shown by the formula, C_4H_4NH.

Iodol is a grayish-brown, bulky powder, more or less crystalline, and free from odor and taste. It contains about 89 per cent. of iodine, and requires about 5000 parts of water for solution, but is quite soluble in alcohol, ether, chloroform, and fixed oils. Its alcoholic solution is miscible with glycerin.

Iodol is the oldest of the iodoform substitutes, having been introduced in 1885.

Other compounds which have been recommended as substitutes for iodoform are *europhen* or di-isobutylorthocresol iodide, $C_{22}H_{29}O_2I$, an amorphous yellow powder; *sozoiodol* or sozoiodolic acid and its salts, $C_6H_2I_2OHSO_3H + 3H_2O$, occurring in crystalline form; *losophane* or tri-iodometacresol, $C_6HI_3OHCH_3$, odorless and colorless crystals containing nearly 80 per cent. of iodine; *sulphaminol* or thioxydiphenylamine, $C_{12}H_9OS_2N$, a yellow insoluble powder.

Hydrated Chloral. $C_2HCl_3O + H_2O$ or $CCl_3COH + H_2O$.—This compound, as indicated in the official title, is a combination of chloral and water. Anhydrous chloral is an oily liquid having the composition CCl_3COH.

In the manufacture of hydrated chloral perfectly dry chlorine gas is passed into cold absolute alcohol as long as the former continues to be rapidly absorbed, after which the mixture is rapidly warmed to 60°–70° C. (140°–158° F.) and treated with sulphuric acid, whereby crude chloral is separated as a thin oily liquid, which is then rectified over burned lime and chalk; the final distillate of pure chloral is weighed and hydrated by the addition of a calculated quantity of water, the hot mass being poured upon plates of glass, covered with a bell-glass and allowed to crystallize.

The reactions occurring in the above process were at one time supposed to consist in the formation of aldehyde and the conversion of this into chloral or trichloraldehyde by the action of chlorine, as illustrated by the equations $C_2H_5OH + Cl_2 = C_2H_4O + 2HCl$ and $C_2H_4O + Cl_6 = CCl_3CHO + 3HCl$. This view is no longer tenable, since it has been found that chlorine brought into contact with aldehyde yields trichlorbutylaldehyde, $C_4H_5Cl_3O$, a condensation-product, instead of chloral. According to recent authorities, the nascent aldehyde produced by the action of chlorine on alcohol acts upon the absolute alcohol present, forming acetal and water ; thus, $2C_2H_5OH + C_2H_4O = C_2H_4(OC_2H_5)_2 + H_2O$; the acetal is converted by chlorine into trichloracetal, $C_2H_4(OC_2H_5)_2 + Cl_6 = C_2HCl_3(OC_2H_5)_2 + 3HCl$, and this is decomposed by the hydrochloric acid present into chloral alcoholate and ethyl chloride; thus, $C_2HCl_3(OC_2H_5)_2 + HCl = C_2HCl_3O.C_2H_5OH + C_2H_5Cl$; finally the chloral alcoholate is decomposed by sulphuric acid into chloral, ethyl sulphuric acid, and water, $C_2HCl_3O.C_2H_5OH + H_2SO_4 = CCl_3CHO + C_2H_5HSO_4 + H_2O$. Other decomposition-products are also formed in small quantities.

In order further to purify the crystals of hydrated chloral, it is customary for manufacturers to decompose again the hydrate with sulphuric acid, whereby pure chloral is set free, and then rectifiy, rehydrate, and recrystallize the product.

Hydrated chloral is readily soluble in water, alcohol, ether, chloroform, fixed and volatile oils. Its solutions are incompatible with caustic alkalies, alkaline earths and ammonia, chloroform and a formate of the base being produced. While aqueous solutions of hydrated chloral are perfectly neutral when freshly prepared they gradually acquire an acid reaction, but alcoholic solutions remain neutral. If hydrated chloral be dispensed together with concrete volatile oils or phenols, liquefaction takes place and the mixture must be thoroughly triturated, preferably in a glass mortar, until a homogeneous liquid results.

Chloral has yielded a number of derivative products which are used to some extent. The most prominent of these is

Chloralformamide. $C_3H_4Cl_3NO_2$ or $CCl_3.CH(OH)NH.COH$.—This compound, which is recognized in the Pharmacopœia, is commercially also known as *chloralamide,* although the latter name properly belongs to another chemical, *chloral-ammonia,* having the composition $CCl_3COH + NH_3$. The official title in the German Pharmacopœia is *chloralum formamidatum.* It is obtained by interaction between anhydrous chloral and formamide $CHONH_2$, a colorless oily liquid produced by dry distillation of urea and ammonium formate, at about 140° C. (284° F.). Chloralformamide occurs in white, lustrous crystals which are slowly soluble in cold water, but are decomposed by water heated to 60° C. (140° F.). It is used as a hypnotic, and must not be confounded with *chloralimide,* a decomposition product of chloralamide mentioned above, formed when the latter is heated.

Other compounds, such as *hypnal*, a compound of chloral and antipyrine, *somnal*, a compound of chloral, urethane, and alcohol, *ural* or *uralium*, chloral-urethane, etc., are less important. A full account of these may be found in the *National Standard Dispensatory*, p. 409.

Closely allied to the official hydrated chloral is *butyl-chloral hydrate*, $C_3H_4Cl_3COH + H_2O$, which is recognized in the British Pharmacopœia, and is in commerce often, although wrongly, called crotonchloral hydrate. It is prepared from ethyl aldehyde by acting upon it with chlorine at a low temperature,—10° C. (14° F.); the mixture is finally subjected to fractional distillation until a product boiling uniformly between 163° and 165° C. (325.4° and 329° F.) is obtained, consisting of trichlorbutylaldehyde or butyl-chloral, which is then converted into the crystalline hydrous variety by addition of water. Butyl-chloral hydrate dissolves sparingly in cold water, but freely in hot water, alcohol, and glycerin. It differs from hydrated chloral in not yielding chloroform with alkalies, but instead dichlorallylene, $C_3H_4Cl_2$.

Bromal, or tribromaldehyde, CBr_3COH, resembles chloral in its chemical nature and like the latter forms a hydrate and an alcoholate. It is prepared from absolute alcohol by the action of bromine, and with caustic alkalies forms bromoform and alkali formate. Bromal must not be confounded with bromol, which is tribromophenol (see under Phenol, page, 620).

Paraldehyde. $(C_2H_4O)_3$.—This liquid is a polymeric form of ethyl aldehyde, which latter is an oxidation-product of alcohol.

Aldehydes, chemically speaking, are derived from primary alcohols, contain the characteristic group COH, and upon further oxidation yield acids. Ethyl aldehyde or acetaldehyde, C_2H_4O or CH_3COH, commonly known as aldehyde in commerce, is a colorless neutral liquid obtained by distilling a mixture of alcohol, water, sulphuric acid, and manganese dioxide or potassium dichromate; the crude product is dissolved in ether and charged with ammonia gas. The resulting crystals of aldehyde-ammonia, $C_2H_4ONH_3$, are distilled with diluted sulphuric acid and rectified over calcium chloride. By condensation of three molecules of aldehyde one of paraldehyde is formed, $3C_2H_4O = C_6H_{12}O_3$.

The latter is usually prepared by passing gaseous hydrochloric acid into aldehyde at ordinary temperature until the liquid is no longer soluble in an equal volume of water. By repeated freezing and distillation the crude product is purified until it finally all volatilizes at 124° C. (355.2° F.). Paraldehyde is a colorless liquid of strong, but not pungent, odor, soluble in 9 parts of water at ordinary temperature and miscible in all proportions with alcohol, ether, and fixed and volatile oils. It is usually dispensed in the form of an emulsion, like ether or chloroform.

Closely allied to acetaldehyde is formaldehyde, HCOH, also known as methyl aldehyde and methylene oxide, which bears the same relation to methyl alcohol as acetaldehyde bears to ethyl alcohol. It is a colorless, pungent gas, obtained by oxidation of methyl alcohol vapor mixed with air. The oxidation is effected by bringing the vapor in contact with moderately heated spirals of copper gauze superficially oxidized. The Pharmacopœia recognizes an aqueous solution of formaldehyde under the Latin title Liquor Formaldehydi, which is also known in commerce as *formalin* and *formol*. The official solution should contain not less than 37 per cent. of formaldehyde, which may be determined volumetrically. The official assay method was first suggested by Blank and Finkenbeiner in 1898 and involves the oxidation of formaldehyde to formic acid at the expense of the hydrogen dioxide added, the acid being neutralized by the alkali hydroxide, and hydrogen being eliminated according to the following reaction: $2HCOH + H_2O_2 + 2NaOH = 2HCOONa + 2H_2O + H_2$. Since 59.58 Gm. of formaldehyde will yield by oxidation sufficient formic acid to neutralize 79.52 Gm. of sodium hydroxide, as shown by the equation above, each Cc. of normal sodium hydroxide solution neutralized by the newly formed formic acid, in the official test, corresponds to 0.02979 Gm. of formaldehyde.

If an aqueous solution of formaldehyde is boiled, a portion of the gas is volatilized, while another portion polymerizes and becomes insoluble, separating as a white flocculent mass, which upon drying has the composition $C_3H_6O_3$ or $(HCOH)_3$, and is chemically known as *trioxymethylene*. Commercially this polymerized formaldehyde is better known as *paraform*, and occurs both in the form of a white powder and in compressed tablets weighing 1 gramme; it is used for disinfecting purposes by being placed in an iron dish and heated, when it splits up again into gaseous formaldehyde, and as such becomes active, possessing also strong germicidal properties. To remove the disagreeable, pungent vapor remaining in rooms after the use of formaldehyde, ammonia water may be used, which combines with the gas, forming a harmless compound, which has been introduced into medicine and is officially recognized as

Hexamethylenamine. $C_6H_{12}N_4$ or $(CH_2)_6N_4$.—This basic compound, the full chemical name of which is hexamethylene tetramine, is also known as *urotropin*, *cystogen*, *formin*, *uritone*, and *aminoform*. It is a condensation product obtained by adding to a strong solution of formaldehyde small successive portions of stronger ammonia water, the mixture being kept well cooled, until an excess of ammonia is indicated by the odor after the solution has stood several hours. The solution is then poured into shallow dishes and allowed to crystallize. The crystals may be further purified by treatment with animal charcoal and subsequent recrystallization. Hexamethylenamine occurs as colorless odorless crystals having a sweetish taste, and soluble in 1½ times their weight of water, the solution showing an alkaline reaction toward litmus.

Several derivatives of hexamethylenamine have been introduced under special names, thus: Hexamethylene-tetramine salicylate, known as *urotropine salicylate* or *saliform;* hexamethylene-tetramine bromethylate, known as *bromalin*, *bromalium*, *bromoformin*, or *bromethylformin;* hexamethylene-tetramine tannin, known as *tannopin* or *tannon;* hexamethylene-tetramine iodoform, known as *iodoformin;* a compound of hexamethylene-tetramine hydrochloride and ferric chloride, known as *ferrostyptin*. Further particulars regarding these preparations may be found in the *National Standard Dispensatory*, pages 761 and 762.

Spirit of Nitrous Ether.—The official preparation recognized by this name is an alcoholic solution of ethyl nitrite, $C_2H_5NO_2$, yielding when freshly prepared and tested by the method of assay given in the Pharmacopœia not less than 4 per cent. of ethyl nitrite.

In the pharmacopœial process of manufacture, which is especially intended for the pharmacist in making small quantities of the spirit, the first step is the preparation of ethly nitrite by acting on a solution of sodium nitrite with sulphuric acid in the presence of alcohol. The nitrous acid liberated attacks the alcohol, forming ethyl nitrite and water. The two reactions are indicated by the following equations: $NaNO_2 + H_2SO_4 = HNO_2 + NaHSO_4$; $C_2H_5OH + HNO_2 = C_2H_5NO_2 + H_2O$. The newly-formed ethyl nitrite rises as an oily layer to the surface and, after all reaction has ceased, is transferred to a glass separator where it is washed first with plain ice-cold water and then with an ice-cold solution of monohydrated sodium carbonate. After careful separation, the ethyl nitrite is freed from water by agitation with anhydrous potassium carbonate and finally mixed with 21 times its weight of alcohol. In order that a large yield of ethyl nitrite may be insured, it is essential that the tube of the separator be allowed to reach nearly to the bottom of the flask containing the alcohol and sulphuric acid mixture, and that the solution of sodium nitrite be allowed to flow into the flask very slowly in drops, the flask being kept thoroughly cold during the reaction. From the above equation it will be seen that 68.57 Gm. of absolute sodium nitrite are capable of yielding 74.51 Gm. of ethyl nitrite, and if the official salt (containing at least 90 per cent. of $NaNO_2$) be used, the 100 Gm. ordered in the official formula should be able to produce at least 97.79 Gm. of ethyl nitrite, which would yield 2151.38 Gm. of the official spirit. In practice there is always some loss, the full theoretical yield being never obtainable, and hence the necessity of ascertaining the exact weight of the purified ethyl nitrite in order to determine the final weight of alcohol to be added. The process is easy of execution and with a little care

$:: 273 + t : 273 + 25$ or $x = \frac{273 + 25}{273 + t}$; that is, 1 Cc. of NO gas at t° C. would become $\frac{273 + 25}{273 + t}$ Cc. at 25° C. The correction in volume for each Cc. of NO gas as read at t° C. thus becomes $\left(1 - \frac{273 + 25}{273 + t}\right)$ Cc. $= \left(\frac{t - 25}{273 + t}\right)$ Cc. when it is greater than 25° C., or $\left(\frac{273 + 25}{273 + t} - 1\right)$ Cc. $= \left(\frac{25 - t}{273 + t}\right)$ Cc. when it is less than 25° C. When the temperature is only a few degrees above or below 25° C. the denominator of these fractions is approximately 300, so that they become $\frac{1}{300}$, $\frac{2}{300}$, $\frac{3}{300}$, etc., according as the difference between temperature t of measurement of the NO gas and 25° C. is 1, 2, 3, etc., degrees. As each Cc. of NO gas measured in the assay is too great or too small by $\frac{1}{300}$ part for each degree of temperature above or below the official temperature, fixed at 25° C., it follows that the per cent. as first calculated must be corrected by $\frac{1}{300}$ (*i. e.*, $\frac{1}{3}$ of 1 per cent.), as given in the Pharmacopœia. This correction deviates more and more from the truth as the temperature difference becomes greater.

If the pressure under which the NO gas is measured is not 760 Mm. of mercury, which is the one assumed in the assay formula for calculation, the volume is either too large or too small, and therefore the per cent. of ethyl nitrite found also. If we let p = pressure in Mm. of mercury under which the NO gas is measured, then, according to Boyle's law—namely, that the product of the volume and pressure of a gas is always constant, 1 Cc. NO gas $\times p = x$ Cc. NO $\times$ 760, or $x = (1 \text{ Cc.} \times p) \div 760$—that is, 1 Cc. NO measured at any other pressure, p, would be $\frac{p}{760}$ Cc. at normal barometic pressure, 760 Mm. The correction in volume for each Cc. NO gas measured at pressure p is $\left(1 - \frac{p}{760}\right)$ Cc. or $\frac{760 - p}{760}$ Cc., when p is less than 760, or $\frac{p - 760}{760}$ Cc. when p is greater than 760. When p is greater than 760 the gas is under too great a pressure—that is, the volume is less than it should be, hence a correction should be added to the calculated per cent. as first found in the official method of calculation. When p is less than 760 the correction must be subtracted. According as the pressure is 1, 2, 3, etc., Mm. of mercury above or below the normal, 760 Mm., the correction for each Cc. of NO gas will amount to 1, 2, 3, etc., times $\frac{1}{760}$, and the correction of the per cent. must be the same number of times $\frac{1}{760}$ of that first found. $\frac{1}{760}$ is sufficiently close to $\frac{1}{750}$ or $\frac{4}{30}$ of $\frac{1}{100}$, which means $\frac{4}{30}$ of 1 per cent., as given in the Pharmacopœia. This correction, as in the case of temperature, is only a close approximation, and must not be construed as absolute.

In place of the gasometric method, volumetric determination of the percentage of ethyl nitrite may be employed, which is readily carried out and is claimed by some to be more accurate than the gasometric estimation. It depends on the interaction of ethyl nitrite with potassium chlorate and subsequent titration of the resulting potassium chloride with silver nitrate, the process being carried out as follows: Into a 100-Cc. flask or bottle of flint glass, pour 10 Cc. of distilled water, 5 Cc. of cold aqueous saturated solution of potassium chlorate, 5 Cc. of spirit of nitrous ether, and 5 Cc. of 10 per cent. nitric acid. Cork quickly and shake the flask or bottle frequently during 30 minutes. Then add 10 Cc. of $\frac{N}{10}$ $AgNO_3$ solution, shake, add 10 Cc. of ferric ammonium sulphate test-solution as indicator, and titrate the excess of silver nitrate solution with $\frac{N}{10}$ KSCN solution. When a permanent reddish color is imparted to the liquid, deduct the number of Cc. of the potassium sulphocyanate solution required from 10 (the number of Cc. of silver nitrate solution added), multiply the remainder by 2.2353 (or 0.022353 × 100) and divide the product by the weight of 5 Cc. of the spirit of nitrous ether previously ascertained; the quotient will represent the percentage of ethyl nitrite in the sample. The reactions involved in the preceding method are: $3C_2H_5NO_2 + KClO_3 = 3C_2H_5NO_3 + KCl$; $KCl + AgNO_3 = AgCl + KNO_3$; which show that 3 molecules or 223.53 parts of ethyl nitrite are capable of producing 1 molecule or 74.04 parts of potassium chloride, and that this in turn requires 1 molecule or 168.69 parts of silver nitrate for complete precipitation. Hence each Cc. of $\frac{N}{10}$ $AgNO_3$ solution, containing 0.016869 Gm. of silver nitrate corresponds to 0.022353 Gm. of ethyl nitrite.

It has been shown by previous investigators that aldehyde has no effect on the results obtained by this method, unless it be present in large quantity, in which case it will lower the results.

Whenever an assay of spirit of nitrous ether is to be made, the latter should be carefully neutralized by agitation with potassium bicarbonate before weighing, as free nitrous acid may be present, which would cause the results of the determination to be recorded too high.

Commercial spirit of nitrous ether is often of very inferior quality, since it is frequently kept in large carboys insecurely stoppered, and consequently becomes oxidized by the air and moisture. It should always be purchased in original packages of small size and preserved in a cool, dark place. The acid reaction observed in some samples of spirit of nitrous ether may be due to acetic acid produced by oxidation of any aldehyde present, or it may be due to decomposition of the ethyl nitrite, resulting in the formation of alcohol and liberation of nitrous acid. Such acidity should invariably be neutralized by means of alkali carbonate before dispensing the spirit in conjunction with alkali iodides, bromides, etc.

Even under the most favorable conditions spirit of nitrous ether gradually deteriorates, and, if found to contain less than 3 per cent.

of ethyl nitrite, should be condemned. Freshly prepared spirit of nitrous ether if carefully preserved in a cool, dark place, will keep unchanged for three or four months. Exposure to diffused daylight and air accelerates decomposition; hence, when purchased in bulk, drawn from half-filled or carelessly stoppered containers, the spirit is often worthless. The author has repeatedly had occasion to examine spirit of nitrous ether offered for sale in bulk by jobbers in different parts of the country, and regrets to say that in only a few cases has the strength found ever approached that required by the Pharmacopœia; in some cases less than 1 per cent. of ethyl nitrite was present.

Amyl Nitrite.—Under this name the Pharmacopœia recognizes a liquid containing about 80 per cent. of true amyl nitrite, $C_5H_{11}NO_2$, together with variable quantities of undetermined compounds. Although not a derivative of official alcohol, this preparation may be conveniently considered at this point, owing to its similarity, chemically, to spirit of nitrous ether. Amyl nitrite is an ester, or ethereal salt, bearing the same relation to amyl alcohol as ethyl nitrite bears to official or ethyl alcohol. It can be prepared by direct action of nitric acid on purified amyl alcohol, but is now probably altogether obtained by distilling a solution of sodium nitrite with amyl alcohol and sulphuric acid, that portion of the distillate coming over between 95° and 100° C. (203° and 212° F.) being collected, washed with ice-cold sodium carbonate solution, dehydrated with anhydrous potassium carbonate, and redistilled below 100° C. (212° F.) According to the equation $2C_5H_{11}OH + 2NaNO_2 + H_2SO_4 = 2C_5H_{11}NO_2 + Na_2SO_4 + 2H_2O$, 116.24 parts of amyl nitrite should be obtained from 87.43 parts of amyl alcohol, but in practice such is not the case.

As amyl nitrite rapidly deteriorates by exposure to air and light, it must be kept in securely closed, small vials, or in sealed bulbs, in a dark place. The commercial article is very variable in quality, samples having been found to contain as little as 28 per cent. of true amyl nitrite and others containing as much as 93 per cent. The assay of amyl nitrite is directed by the Pharmacopœia to be made gasometrically, as in the case of spirit of nitrous ether, 3 Cc. of the amyl nitrite, which has previously been made perfectly neutral by agitation with potassium bicarbonate and then decanted, being carefully weighed and then diluted with sufficient alcohol to produce 100 Cc. of liquid; of this solution 10 Cc. are used for the assay, representing exactly $\frac{1}{10}$ of the original quantity of amyl nitrite. The volume of gas collected is multiplied by 4.8 (or 0.047851×100) and the product divided by the weight of amyl nitrite used in the test ($\frac{1}{10}$ of the weight of the 3 Cc.) to find the percentage.

As in the case of spirit of nitrous ether, amyl nitrite may also be assayed volumetrically by the method described on page 661. 5 Gm. of amyl nitrite are dissolved in sufficient alcohol to make 100 Cc. and of this solution 10 Cc. are used for the test. The number of Cc. of $\frac{N}{10}$ AgNO solution required for precipitation is multiplied by 3.4872 (or 0.034872 × 100) and the product divided by 0.5 (the weight in grammes of amyl nitrite used) to find the percentage of true amyl nitrite in the sample. From the equations $3C_5H_{11}NO_2 + KClO_3 = 3C_5H_{11}NO_3 + KCl$, and $KCl + AgNO_3 = AgCl + KNO_3$ it is seen that 3 molecules or 348.72 parts of amyl nitrite will require 1 molecule or 168.69 parts of silver nitrate for precipation of the potassium chloride formed, and hence 1 Cc. of $\frac{N}{10}$ $AgNO_3$ solution, containing 0.016869 Gm. of silver nitrate, corresponds to 0.034872 Gm. of amyl nitrite.

Amyl Alcohol, although not recognized in the Pharmacopœia, is of interest as the source of amyl nitrite and valeric acid and as a valuable solvent used in chemical research. As stated on page 642, amyl alcohol and other homologous products are formed during the fermentation of grain or potato starch; larger quantities may be obtained by continuing the distillation after ethyl alcohol ceases to come over. Amyl alcohol is purified by fractional distillation and repeated washing with a concentrated solution of table salt. It is a colorless, thin, oily liquid of about the same specific gravity as alcohol, but boiling, when pure, at 132° C. (269.6° F.). Chemically, it is amyl hydroxide, $C_5H_{11}OH$, and yields compounds homologous with those of ethyl alcohol, namely, amyl ether, $(C_5H_{11})_2O$, amyl aldehyde, $C_5H_{10}O$, and valeric acid, $C_5H_{10}O_2$. Amyl alcohol, obtained in the fermentation of grain or potato starch, is designated by chemists as primary iso-amyl alcohol, and is the chief constituent of commercial fusel oil. It is only slightly soluble in water, but is miscible with alcohol and ether in all proportions.

CHAPTER LVII.

FATS AND FIXED OILS.

THE physical properties of these compounds have been considered on pages 202–203. Chemically, they belong to the class of esters, or ethereal salts, being chiefly glycerides of fatty acids, and readily resolved into the respective acids and alcohols by means of alkali hydroxides. The constitution of fats and fixed oils was first studied and announced by Chevreul in 1811. With a few exceptions, the basylous radical is the same for all fats and fixed oils, whether obtained from the vegetable or animal kingdom, namely, glyceryl or propenyl, C_3H_5, a trivalent group derived from the hydrocarbon propane, C_3H_8, the alcohol or hydroxide of which is glycerin or propenyl alcohol, $C_3H_5(OH)_3$; other bases obtainable from fats are myricyl alcohol, $C_{30}H_{61}OH$, cetyl alcohol, $C_{16}H_{33}OH$, ceryl alcohol, $C_{26}H_{53}OH$, cholesterin (from animal fats), $C_{26}H_{43}OH$, phytosterin (from vegetable fats), $C_{26}H_{43}OH$, and others. The acid radicals found in fats are many, the chief ones being arachidic acid, $HC_{20}H_{39}O_2$, butyric acid, $HC_4H_7O_2$, capric acid, $HC_{10}H_{19}O_2$, capronic acid, $HC_6H_{11}O_2$, caprylic acid, $HC_8H_{15}O_2$, cerotic acid, $HC_{26}H_{51}O_2$, erucic acid, $HC_{22}H_{41}O_2$, lauric acid, $HC_{12}H_{23}O_2$, linolenic acid, $HC_{18}H_{29}O_2$, linolic acid, $HC_{18}H_{31}O_2$, melissic acid, $HC_{30}H_{59}O_2$, myristic acid, $HC_{14}H_{27}O_2$, oleic acid, $HC_{18}H_{33}O_2$, palmitic acid, $HC_{16}H_{31}O_2$, stearic acid, $HC_{18}H_{35}O_2$, tiglic acid, $HC_5H_7O_2$, etc., varying from one to three or four in number for a single fat or fixed oil.

The ordinary fats and oils used in pharmacy consist, for the most part, of two or three compound ethers, to which the names olein, palmitin, and stearin have been given; of these, olein, being always liquid, naturally forms the chief constituent of fixed oils, while palmitin and stearin, being solid at ordinary temperatures, by their presence determine the firmer consistence of solid fats. All three are fatty acid esters of glyceryl, known respectively to chemists as glyceryl trioleate, $C_3H_5(C_{18}H_{33}O_2)_3$, glyceryl tripalmitate, $C_3H_5(C_{16}H_{31}O_2)_3$, and glyceryl tristearate, $C_3H_5(C_{18}H_{35}O_2)_3$. The oleic acids derived from different oils, not having a uniform composition and properties, specific names are employed to distinguish the respective glycerides; thus, olein, linolein, and physetolein; the first-named occurs both in animal and vegetable fats, the second only in vegetable fats, while the third is confined to animal fats, chiefly fish-oil, seal oil, etc.

When absolutely pure, fats and fixed oils are without action on litmus, but in the presence of air, light, and moisture decomposition and oxidation gradually ensue, an unpleasant odor, due to the formation of volatile products, and an acid reaction being observed. Fats are not affected by a temperature of 100° C. (212° F.) but at 250° C. (482° F.) they are decomposed, various volatile products being formed, among which is an irritating, odorous substance, called acrolein, which, chemically, is allyl aldehyde, C_3H_4O or CH_2CHCOH, and is derived from the decomposition of the glycerin present in fats.

Non-drying oils, consisting chiefly of the glyceride of oleic acid, with varying proportions of palmitin, upon exposure to air, appear to absorb water and split up into free oleic (and palmitic) acid and glycerin, the latter being oxidized gradually into carbon dioxide and water, and thus disappearing. The oleic acid absorbs oxygen and is gradually converted into oxystearic acid, and finally into volatile odorous acids, such as capronic, valeric, etc. This process of decomposition is termed rancidification, and explains the condition termed rancidity noticed in old and carelessly preserved fats and fixed oils. By some it is thought that the change is superinduced by the presence of mucilaginous or albuminous matter in the fat, acting as a ferment under the influence of light, air, and moisture. Rancid fats, therefore, always contain free acid and yield less glycerin than sweet fats when saponified.

In the chemical examination of fats and fixed oils for adulterations, and as tests of identity, two reactions, largely used by analysts, have been adopted by the Pharmacopœia, namely, that with potassium hydroxide and that with iodine. Both tests are applied to every official fixed oil and definite requirements made in connection with the same. The test with potassium hydroxide is better known as the determination of the saponification value or Koettstorfer number, being the number of milligrammes of potassium hydroxide required for complete saponification of 1 Gm. of a fat or oil, and is carried out as follows: Weigh out accurately in a flask, holding 150 to 200 Cc., 1.5–2 Gm. of the purified and filtered fat. Next run into the flask from a burette, 25 Cc. of alcoholic potassium hydroxide test-solution. While exactly 25 Cc. is not indispensable, in comparative tests precisely the same amount must be used, allowing the burette to drain in exactly the same way in each test. Then place a small funnel in the flask and heat it on a water-bath containing boiling water for ½ hour, so that the alcohol is simmering, frequently imparting a rotatory motion to the contents of the flask. Then add 1 Cc. of phenolphthalein test-solution and titrate back the excess of potassium hydroxide with half-normal hydrochloric acid. If a blank test is made at the same time with the alcoholic potassium hydroxide test-solution alone, the difference in the number of Cc. of half-normal hydrochloric acid consumed by the blank test and the real test, multiplied by 27.87 (being the number of milligrammes of KOH contained in each Cc. of the alcoholic potassium hydroxide test-solution, which is a half-normal solution) and divided by the weight in grammes of the fat or oil, will give the saponification value of the sample tested. In some cases prolonged boiling is necessary to effect perfect saponification, occasionally 2 or 3 hours being required, and a reflux condenser or long glass tube passing through a cork will be found preferable to a glass funnel for preventing the loss of alcohol.

The test with iodine consists in determining the iodine value or number, which is a figure indicating the number of grammes of iodine absorbed by 100 Gm. of a fat or oil under certain conditions. The figure is also known as Huebl's iodine number, and is based upon the saturation with iodine of unsaturated fatty acids and their glycerides in the presence of an alcoholic solution of mercuric chloride, whereby colorless addition compounds are produced. The following are the official directions for applying the test: To a solution of 0.3 Gm. (0.15–0.2 Gm. for linseed oil and 0.8 Gm. for oil of theobroma and similar fats), of the fat or oil in 10 Cc. of chloroform contained in a glass-stoppered bottle of 250 Cc. capacity, add 25 Cc. of a mixture of equal volumes of alcoholic iodine test-solution (25 Gm. of iodine in 500 Cc. of alcohol), and alcoholic mercuric chloride test-solution (30 Gm. of mercuric chloride in 500 Cc. of alcohol), both of which have been measured from a burette. After having been securely stoppered, the bottle is set aside in a cool place, protected from the light for a period of 4 hours (16 hours are required for accuracy in the case of linseed oil). After this time, the mixture must still possess a brown color; if it does not, a further measured portion of the mixture of the two reagents should be added, and the mixture again set aside. Finally, 20 Cc. of potassium iodide solution are added, followed by 50 Cc. of water, and $\frac{N}{10}$ sodium thiosulphate solution is then added in small successive portions, shaking thoroughly after each addition until the color of the mixture is discharged. The number of Cc. of the sodium thiosulphate solution is noted. At the same time that this test is carried out, a blank experiment is made, in which exactly the same quantities of chloroform, iodine test-solution, and mercuric chloride solution are mixed, and after standing for 4 or more hours, the free iodine is estimated by titration with $\frac{N}{10}$ sodium thiosulphate solution as directed above. The number of Cc. of the thiosulphate solution consumed is noted, and from this is deducted the number of Cc. of the thiosulphate which was consumed in the test; the difference multiplied by 12.59 (being the number of Gm. of iodine corresponding to 1000 Cc. of $\frac{N}{10}$ sodium thiosulphate solution), and this product divided by ten times the weight of fat or oil taken, expresses the iodine number of the fat or oil. Instead of multiplying the difference as ordered in the official directions, it may be multiplied by 0.01259 (the weight in Gm. of iodine corresponding to 1 Cc. of the thiosulphate solution), and thus the total weight of iodine absorbed by the fat ascertained, which weight must then be multiplied by 100, and the product divided by the exact weight of fat or oil taken for the test, for the weight of fat or oil taken is to the weight of iodine absorbed as 100

Gm. of fat or oil would be to x, representing the weight of iodine which would be absorbed by the 100 Gm.

The action of acids on fats and fixed oils varies considerably; thus, strong hydrochloric acid has no effect upon them, as also cold diluted nitric acid and cold or hot diluted sulphuric acid. Nitrous acid, as well as warm nitric acid, converts olein into elaidin, a compound isomeric with it, but of firm consistence. Strong sulphuric acid decomposes fats slowly in the cold and rapidly with the aid of heat, forming sulpho-compounds of the fatty acids, as well as of the glycerin. If concentrated sulphuric acid be added to almond or olive oil and the mixture kept at a temperature below 50° C. (122° F.), sulpho-oleic and glycerylsulphuric acids will be formed, $HSO_3C_{18}H_{33}O_2$ and $C_3H_5(HSO_4)_3$; if castor oil be used, sulpho-ricinoleic acid will be produced. The glycerylsulphuric acid upon addition of water is again converted into glycerin and sulphuric acid, and can thus be removed; the sulpho-oleic acid, having been purified by washing with salt solution, can be combined with alkali hydroxides, yielding water-miscible sulpho-oleates, which on account of their absorbability have been recommended as vehicles for ointments, under the names oleite, polysolve, etc. (see page 414.

THE OFFICIAL FATS AND FIXED OILS.

Almond Oil (Expressed).—This oil consists of about 85 per cent. of olein, mixed with palmitin, but is said to be free from stearin, which accounts for the fact that the oil can be cooled to —20° C. (—4° F.) before congealing. Although olive oil, cottonseed oil, lard oil, and sesame oil may be present in commercial almond oil, these can be detected by cooling to —10° C. (14° F.), but the presence of apricot or peach-kernel oil is not shown by this test, as both remain fluid even at —20° C. (—4° F.). The latter may be detected by mixing almond oil with an equal volume of nitric acid and water, when a white mass free from red color should be obtained; a brown color would indicate the presence of cottonseed and sesame oils.

The saponification value of expressed oil of almond, according to the Pharmacopœia, should be 191–200, and the iodine number not less than 95 and not more than 100.

Castor Oil.—The chief constituent of this well-known oil is triricinolein, $C_3H_5(C_{18}H_{33}O_3)_3$, together with ricinisolein, palmitin, and dioxystearin. Ricinolein differs from olein in being the glyceride of an acid containing in each molecule one atom more of oxygen than oleic acid. As already stated on page 208, castor oil differs from other fatty oils in its marked solubility in absolute and official alcohol; it is also immiscible with more than its own volume of petroleum benzin or 1½ times its volume of mineral oils. The specific the liquid assumes a permanent pink tint. Note the number of Cc. of alkali solution used, and multiply this by 0.141, which will give the amount of free fatty acid present in the given weight of oil, calculated as oleic acid. Divide the product thus obtained by the weight of oil taken, and multiply the quotient by 100, to find the percentage of free acid.

The Pharmacopœia requires that codliver oil shall show a saponification value of 175–185 and an iodine number not less than 140 nor more than 150. According to Gane, if the time allowed for absorption of the iodine be extended to 6 hours, genuine codliver oil will take up from 150 to 170 per cent. of the same.

Cottonseed Oil.—This oil consists chiefly of olein, palmitin, and linolein, together with small quantities of the glycerides of linolenic acid and coloring matter, which latter is removed by bleaching the oil with warm weak solutions of alkali hydroxide. Cottonseed oil when saponified with alcoholic potassium hydroxide solution should show a saponification value of 191–196. The Pharmacopœia gives the iodine number as not less than 102 nor more than 108. The presence of cottonseed oil in other oils may be detected by Halphen's test and the test with silver nitrate, as explained under Lard, on page 671. Nitric acid of 1.375 specific gravity produces a deep-brown coloration with cottonseed oil, the coloration being more or less vitiated, however, if the oil has been heated to 240° C. (464° F.).

Croton Oil.—The composition of croton oil is very complex, the glycerides of not less than 10 acids having been found—namely, of oleic, palmitic, stearic, myristic, lauric, valeric, formic, butyric, acetic, and tiglic acids, besides which crotonoleic acid, as yet but little studied, is said to be present both in the free and combined state; this latter acid differs from oleic acid in that its barium salt is soluble in alcohol. The vesicant principle of croton oil was determined in 1895 by Dunstan and Boole, of England, and found to be a bright yellow, hard, brittle substance, to which they gave the name croton resin, and which has the composition $C_{13}H_{18}O_4$; it is soluble in alcohol, ether, and chloroform, and possesses neither acid nor basic properties. Croton oil differs from castor oil in its perfect solubility in petroleum benzin. Its saponification value is given by the Pharmacopœia as 212–218, and its iodine number as not less than 102 nor more than 105.

Lard.—The most important constituents of lard are olein, about 60 per cent. and stearin, about 40 per cent., together with small and variable amounts of palmitin. Lard sometimes contains free fatty acids, but these are limited by the Pharmacopœia to 0.56 per cent., as shown by the test that 10 Gm. of the lard dissolved in chloroform shall not require more than 0.2 Cc. of normal potassium hydroxide solution to produce a pink color, phenolphthalein being used as an indicator.

The presence of cottonseed oil is officially detected by means of an alcoholic solution of silver nitrate acidulated with nitric acid, when no reddish or brown color should be observed. In addition to this test the Pharmacopœia also directs that Halphen's test shall be applied, which consists in mixing melted lard with an equal volume of a mixture of amyl alcohol and a 1 per cent. solution of sulphur in carbon disulphide, and then heating the mixture for 15 minutes in a bath of boiling salt-water, when no reddish color should be developed. According to L. Tolman, the test is made more reliable by continuing the heat for 1 or 2 hours.

Lard Oil.—This oil consists almost wholly of olein, the variable proportions of stearin and palmitin present depending upon the care with which the oil has been expressed. It is subject to adulteration with cottonseed oil and mineral oils. The former may be detected as stated above, under Lard, and the mineral oils by the separation of an oily layer if the lard oil be saponified with alcoholic potassium hydroxide solution. The Pharmacopœia gives the saponification value of lard oil as 195–197, and its iodine number as not less than 56 nor more than 74.

Linseed Oil.—While linseed oil contains small proportions of olein, palmitin, myristin, and stearin, it consists chiefly of the glycerides of linolic acid, $HC_{18}H_{31}O_2$, and linolenic acid, $HC_{18}H_{29}O_2$. Formerly, the name linoleic acid was applied to the fatty acid present in largest amount, but this has been shown to be a mixture of oleic, linolic, linolenic, and isolinolenic acids. Upon exposure of linseed oil to the air, oxidation takes place and oxylinolein is formed, producing a hard varnish-like residue. Since pure linseed oil requires several days for perfect drying, its siccative properties are increased by boiling the oil and by addition of lead oxide, manganese oxide and similar substances. The glyceride of oleic acid present in linseed oil behaves like that of the non-drying oils when the oil is exposed to air, but decomposition is probably estopped by the formation of the other oxidation products; hence the acidity and unpleasant odor due to rancidification are not observed. As already stated on page 209, boiled linseed oil should never be used for pharmaceutical purposes.

Linseed oil may be adulterated with rosin oil and mineral oils, which will remain as an oily residue if the oil is saponified with alcoholic solution of potassium hydroxide; the resulting soap must be completely soluble in water. The Pharmacopœia gives the saponification value of linseed oil as 187–195, and the iodine number as not less than 170; the latter is rarely below 175 and varies with oils from different sources, sometimes running as high as 190 and even 198.

Olive Oil.—This oil consists of 72 per cent. of liquid glycerides (a mixture of olein, 94 parts, and linolein, 6 parts) and 28 per cent. of solid glycerides, chiefly palmitin with small quantities of arachin. The unsaponifiable matter met with in olive oil has been shown to be phytosterin, and the greenish color of the oil is due to chlorophyl from the olive fruit. Olive oil has been found adulterated with cottonseed, peanut and sesame oils, for the detection of which the Pharmacopœia gives appropriate tests. According to Tolman, olive oil contains an impurity which interferes with the tests for cottonseed and sesame oils, and hence all olive oil should first be thoroughly shaken with hot alcohol and then washed with hot water before the official tests are applied. The same authority recommends that during the application of Halphen's test (see under Lard, page 671), the heat should be continued for 1 or 2 hours, as cottonseed oil which has been heated will respond to this test only after 1 or 2 hours, and would escape detection during the short period directed in the official test.

The most extensively met-with adulteration is, perhaps, peanut oil, and its detection is more difficult than that of other oils, since its chemical and physical constants are very similar to those of olive oil. The test used by the Bureau of Chemistry of the Agricultural Department at Washington, D. C., which depends upon the determination of arachidic acid, and is given in detail in the *National Standard Dispensatory*, page 1094, is said to yield very satisfactory results; 20 times the weight of arachadic acid obtained will approximately indicate the amount of peanut oil present.

The Pharmacopœia gives the saponification value of olive oil as 191–195, and its iodine number as not less than 80 nor more than 88.

Oil of Theobroma.—Cacao butter, by which name this oil is better known, is composed of the glycerides of oleic, stearic, palmitic, and lauric acids, together with small quantities of the glycerides of butyric, formic, linolic, and arachidic acids. A peculiar feature of oil of theobroma is that the specific gravity of recently melted and congealed oil is lower than the normal, the maximum specific gravity not being attained for some time after (from 1 to 3 weeks).

The most probable adulterations of oil of theobroma are wax, stearin, and tallow, for the detection of which the official test with solution in ether is admirably adapted. Under the conditions named in the Pharmacopœia, a solution of pure oil of theobroma will not become turbid or separate granular flocculi in less than 3 minutes and form a clear liquid again at 15° C. (59° F.).

Oil of theobroma, if pure, has a saponification value of 188–195, and its iodine number should be not less than 33 nor more than 38.

Spermaceti.—Although composed chiefly of cetyl palmitate, spermaceti contains also glycerides of lauric, myristic, and stearic acids, and is therefore more nearly related to the true fats than wool fat and beeswax. The cetyl palmitate may be separated from the glycerides by recrystallization from alcohol, and when thus purified will not yield vapors of acrolein when heated strongly, whereas ordinary spermaceti does give off the characteristic irritating vapors due to decomposition of glycerin. Spermaceti is readily saponified by means of alcoholic solution of potassium hydroxide, the resulting liquid yielding cetyl alcohol upon addition of water. It is not usually adulterated, since the addition of other fats would materially alter its physical properties, and detection thus not be difficult.

Suet.—Mutton suet, according to Chevreul, consists of 70–80 per cent. of stearin and palmitin, and 20–30 per cent. of olein, together with a trace of hircin, which latter is the glyceride of hircic acid, having a strong acid reaction and a peculiar goat-like odor. The Pharmacopœia recognizes only the prepared or purified suet (see page 207).

Wax.—Beeswax, which is the only kind of wax officially recognized, is a mixture of myricyl palmitate and free cerotic acid, and is said to contain also ceryl palmitate and free melissic acid. It is subject to frequent adulteration with tallow, Japan wax, rosin, paraffin, and ceresin, all of which can be detected by the tests given in the Pharmacopœia. Pure beeswax contains no glycerides, and hence yields no glycerin. The saponification value of yellow wax is officially given as 90–96; in pure wax this is rarely found below 95. Experience has shown that in the saponification test for wax, the time given in the Pharmacopœia for boiling the wax with the alcoholic solution of potassium hydroxide is insufficient, from 1½ to 3 hours' boiling being required to effect perfect saponification. A sample of wax thus treated, which after 1½ hours' time showed a saponification value of 65, after 3 hours gave a value of 94.08, and the longer time would therefore seem preferable for all tests of wax in order to secure accurate results.

Wool Fat.—Natural wool fat is more closely related to the group of waxes than to that of true fats. It is a complex mixture of free fatty acids, palmitic and cerotic acid esters of cholesterin, isocholesterin, and ceryl alcohol, and non-saponifiable bodies, but contains no glycerin. The purified or official fat is obtained, as already stated on page 207, by treatment of the natural fat from wool with weak alkali solution, subsequent washing with water, precipitation with calcium chloride, dehydration with lime and extraction with acetone. After distillation of the solvent, the purified fat thus obtained consists chiefly of cholesterin esters, and should be free from alkalies and free fatty acids. The Pharmacopœia also demands the absence of nitrogenous matter, as shown by boiling wool fat with potassium hydroxide solution, when no vapors of ammonia should be given off.

A characteristic test for the cholesterin esters present in wool fat is Liebermann's cholestol reaction: 1 Gm. of the fat is dissolved in 3–4 Cc. of acetic anhydride, **not** anhydrous acetic acid, and 6 drops of concentrated sulphuric acid gradually added, when a pink coloration will appear, changing to green or blue.

Saponification.—Alkali hydroxides and moist metallic oxides, in the cold, only partly decompose fats and fixed oils, forming emulsions with them, as shown in the case of the official ammonia and lime liniments; but at boiling temperature complete dissociation is effected, the fatty acids combining with the metallic base, while glycerin is liberated. The new compounds thus obtained are known as soap, and the process is termed saponification; the character of the soap depends upon the particular hydroxide employed, sodium hydroxide invariably forming hard soap, while potassium-hydroxide and ammonia form soft soap. The process of saponification may be illustrated by the following equation $C_3H_5(C_{18}H_{33}O_2)_3 + 3NaOH = 3NaC_{18}H_{33}O_2 + C_3H_5(OH)_3$, which represents the manufacture of hard soap from olive oil.

In the manufacture of soap it is customary to add the alkali solution in slight excess to the fat, in order to insure complete decomposition of the latter, the excess remaining in solution. Boiling of the mixture is continued until it becomes transparent and somewhat tenacious, showing that no uncombined fat remains; this is necessary, as the decomposition of the fat is gradual, and the newly formed soap serves as an emulsifying agent for the fat. As the process nears completion iridescent bubbles are seen to rise on the surface, consisting of soap solution. Finally, common salt is added to the finished solution, whereby the soap is precipitated, and can then be drained and allowed to dry in suitable moulds. This explains the fact that ordinary soap will cause no lather with sea water, a special soap made with cocoanut oil or rosin, and known as *marine soap*, being preferable for this purpose, since it is soluble in solution of salt. Since all fats contain some palmitin or stearin (even the fixed oils), the consistence of the soap will depend in part upon the proportion of solid fats present, being firmest in soaps made partly with stearin fats, such as suet, tallow, etc.

The term saponification is used also to express the decomposition of fats and fixed oils by water with the aid of superheated steam, which results in liberation of the fatty acids and glycerin, as in the case of tallow or suet; thus, $C_3H_5(C_{18}H_{35}O_2)_3 + 3H_2O = 3HC_{18}H_{35}O_2 + C_3H_5(OH)_3$. Chemists, not confining the process to the glycerides of fatty acids, further apply the term to the resolution of all compound ethers by an alkali into the respective acids and alcohols, which is often practised in connection with the determination of certain constituents of volatile oils. The action of potassium hydroxide on aldehyde, resulting in the formation of aldehyde-resin, has also sometimes, but erroneously, been called saponification. It pharmacy the term soap is always restricted to the alkali salts of fatty acids, obtained by treatment of a fat or fixed oil with a boiling solution of sodium or potassium hydroxide, which are soluble in water; the name oleate or plaster is more properly applied to those soaps which are insoluble in water or alcohol and are made with the oxides of the earths or heavy metals. Soap made wholly from animal fat is but sparingly soluble in cold alcohol, and is therefore to be preferred for the preparation of solid opodeldoc and similar firm liniments. Such a soap is recognized in the British Pharmacopœia as *Sapo Animalis* or *Curd Soap*.

Medicated Soaps.—While soaps intended simply as detergents may, without detriment, contain a very slight excess of alkali, it is desirable when medication of the soap is intended, that prior to its application a perfectly neutral substance be employed; it has, in fact, been found that soap containing uncombined fat is even preferable to neutral or normal soap, for not only does it render the skin softer, but reaction between the soap and any medicinal agent added is also thereby avoided or at least retarded. Such soaps, containing an excess of fat, are known as *superfatted soaps*, and have been largely used for the past fifteen or twenty years. In preparing them it is customary to add an excess of 3 or 5 per cent. of fat or fixed oil in the beginning of the operation, which then remains intimately mixed with the newly formed soap. In a few cases the excess of fat has been incorporated with the freshly made, neutral soap while yet in a soft, pasty condition. Both olive oil and lanolin are used in the manufacture of superfatted soaps, having been found preferable to all other fats in their action on the skin and toward chemicals.

In the manufacture of medicated soaps the plan followed is identical with that prescribed on page 416 for ointments. The medicinal agent is first intimately mixed (either in the form of solution or impalpably fine powder) with a small portion of the superfatted soap, by means of suitable apparatus, which mixture is then added to such a further quantity of the same vehicle as may be necessary to establish the required percentage strength of the finished product. Among the various medications of superfatted soaps are tar 5 per cent., sulphur 10 per cent., salicylic acid 5 per cent., borax 5 per cent., carbolic acid 5 and 10 per cent., corrosive sublimate 0.1 and 0.5 per cent., camphor 5 per cent., and others.

Official Soaps.—The Pharmacopœia recognizes two varieties of soaps; one by the general name *soap* (Latin, *sapo*), and the other by the general name *soft soap* (Latin, *sapo mollis*). The first is intended to be a hard soap made from olive oil and sodium hydroxide, as already explained. When fresh, or if kept in a damp cellar, it usually contains a large proportion of water, most of which is driven off by drying in a warm, airy room, and all of which can be expelled at a temperature of 110° C. (230° F.). White Castile soap, the kind officially recognized, usually contains a slight excess of alkali, which should not, however, exceed 3 per cent. of sodium carbonate or 0.238 + per cent. of sodium hydroxide, as indicated by the official test with $\frac{N}{10}$ oxalic acid solution. The Pharmacopœia also demands the absence of more than 1 per cent. of matter insoluble in water.

The soft soap of the Pharmacopœia is directed to be made by the action of potassium hydroxide on linseed oil. Commercially, it is generally known as green soap, which was formerly also the official title; the color is, however, by no means green, being yellowish brown. On account of the unsightly appearance and disagreeable odor of the official preparation, the use of olive oil in place of linseed oil has been recommended, yielding a more satisfactory product. The quantity of potassium hydroxide directed in the official formula is based on the assumption that it contains 85 per cent. of absolute KOH; potassium hydroxide of any other strength may be used, and the exact quantity ascertained by dividing 8075 by the percentage of purity. If p be allowed to represent the unknown percentage, and x the unknown quantity, then $p : 85 :: 95 : x$, and $x = 95 \times 85$ (or $8075) \div p$. The value of the official soft soap is partly due to its greater alkalinity. In the German Pharmacopœia this soap is known as *sapo kalinus*.

Glycerin.—As already stated, the basylous radical found in all true fats and fixed oils, both of vegetable and animal origin, is glyceryl, the hydroxide of which is glycerin, $C_3H_5(OH)_3$, a triatomic alcohol. It has proved a most valuable solvent and antiseptic in pharmacy, second only to alcohol in this respect. Nearly all glycerin now produced in this country is made by decomposing fats in large copper digesters; fat and water having been put into the digester, steam under 120 to 150 pounds pressure is introduced for several hours, whereby the mixture is kept in constant agitation and the fat is completely decomposed, the glycerin entering into solution in the water, and the non-volatile fatty acids floating on the surface of the aqueous solution. The volatile fatty acids are allowed to escape with steam through a small orifice in the top of the digester. The dilute solution of glycerin is transferred to evaporating-tanks and concentrated until it reaches a density of 28° Baumé, equal to a specific gravity of 1.24 at 15° C. (59° F.). The crude dark amber-colored glycerin thus obtained is introduced into specially constructed stills, into which steam enters at a temperature of about 250° C. (482° F.), carrying the glycerin, in the form of vapor, with steam, over into a series of condensers so arranged that the glycerin condenses in passing through at various degrees of density; the first condenser, being least cooled, contains the heaviest glycerin, the distillate becoming gradually weaker, until in the last condenser almost pure water is collected. Coloring-matter is removed by treatment with animal or vegetable charcoal, and the distillation is repeated two or three times until the required degree of purity has been obtained. The Pharmacopœia demands at least 95 per cent. of absolute glycerin, which liquid has the specific gravity of 1.246 at 25° C. (77° F.), and is soluble in water and alcohol in all proportions, as also in a mixture of 3 parts of alcohol and 1 part of ether, but is insoluble in ether, chloroform, benzene, petroleum benzin, fixed and volatile oils. The most important tests of those mentioned in the Pharmacopœia are: the absence of turbidity and color when glycerin, after dilution with water, is mixed with silver ammonium nitrate test-solution and then allowed to stand, protected from light, for five minutes; the absence of an offensive or acidulous odor when glycerin is heated with diluted sulphuric acid; the absence of a color darker than yellow, when a mixture of equal volumes of glycerin and concentrated sulphuric acid is allowed to stand for 1 hour; and the complete volatility of glycerin upon ignition. Although official glycerin boils at about 165° C. (329° F.), it is readily vaporized from an aqueous solution at 100° C. (212° F.).

While glycerin is unaffected by cold nitric or sulphuric acid separately, a mixture of the two acids forms with it a definite chemical compound, glyceryl or propenyl trinitrate, $C_3H_5(NO_3)_3$, commonly but wrongly called nitroglycerin, and known also as glonoin and trinitrin. Glyceryl trinitrate is prepared by adding a mixture of 100 parts of anhydrous glycerin and 3 parts of sulphuric acid (spec. grav. 1.835), gradually and in small portions at a time, to a well-chilled mixture of 280 parts of nitric acid (spec. grav. 1.5) and 300 parts of sulphuric acid (spec. grav. 1.835), the vessel being kept surrounded by ice. This mixture is afterward poured into six times its volume of cold water, washed free from acid, and finally dried over sulphuric acid. The reaction may be illustrated as follows: $C_3H_5(OH)_3 + 3HNO_3 + H_2SO_4 = C_3H_5(NO_3)_3 + 3H_2O + H_2SO_4$, the sulphuric acid simply serving to withdraw the water eliminated in the formation of the compound ether. The product is a slightly yellowish, oily liquid, insoluble in water but soluble in alcohol. It has a sweet, aromatic taste, and is very poisonous. In the form of a 1 per cent. alcoholic solution glyceryl trinitrate is recognized in the Pharmacopœia as *Spiritus Glycerylis Nitratis*—Spirit of Glyceryl Trinitrate, or Spirit of Nitroglycerin; tablet triturates and chocolate tablets containing 0.00065 and 0.0013 Gm. ($\frac{1}{100}$ and $\frac{1}{50}$ grain) of glyceryl trinitrate each are also used by physicians; mixed with three parts of infusorial earth (kieselguhr), it constitutes dynamite, a well-known blasting agent.

Glycerophosphoric acid or glycerin acid phosphate, $C_3H_5(OH)_2H_2PO_4$, is another derivative of glycerin introduced into medicine and pharmacy within recent years. It is chiefly used in the form of calcium, iron, or sodium salts. The commercial acid is a 20 per cent. aqueous solution, as all efforts to concentrate the solution and obtain the pure acid have failed, and always resulted in decomposition. When glacial phosphoric acid is gradually dissolved in an equal weight of 95 per cent. glycerin with the aid of moderate heat and the solution then heated in a paraffin-bath for several hours at 100°–110° C. (212°–230° F.), water is split off and a new compound results in the form of a tenacious mass, which is then dissolved in water and neutralized with milk of lime or solution of barium hydroxide. Some calcium phosphate (or barium phosphate) will deposit, and is removed by filtration. The remaining solution is concentrated in a vacuum apparatus, and upon addition of alcohol the glycerophosphate is precipitated and then freed from adhering glycerin by washing with alcohol. For obtaining the commercial acid, the barium glycerophosphate is decomposed with a calculated quantity of diluted sulphuric acid and the resulting barium sulphate removed by filtration.

Petroleum Products.—Pharmaceutically closely allied to the fats, but chemically entirely distinct, are those mixtures of hydrocarbons of the paraffin series obtained by purification of the residuum from the distillation of American petroleum. They are recognized in the Pharmacopœia by the names Paraffin, Petrolatum, Liquid Petrolatum, and White Petrolatum. The British and German Pharmacopœias employ only the name Paraffin, but recognize three varieties of the same as hard, liquid, and soft paraffin. Several of these substances are fat-like in appearance and extensively employed as vehicles for the application of numerous remedial agents; commercially they are known as vaseline, cosmoline, albolene, petrolina, etc.

The existence of petroleum in the earth has not as yet been satisfactorily explained; several theories have been advanced, the most acceptable of which is that petroleum is the result of dissociation of large quantities of fatty matter (derived from marine animals), while under long-continued pressure, at a moderate temperature, with entire exclusion of air.

American petroleum consists of a mixture of hydrocarbons of the fatty or marsh-gas series from methane upward to those richest in carbon, together with small and varying proportions of aromatic hydrocarbons. Upon subjecting the crude petroleum to a refining process by fractional distillation, benzin or naphtha, illuminating-oils, and a residuum largely composed of paraffins are obtained. All fractions are then further purified by treatment with sulphuric acid and subsequently with alkalies, after which they are subjected to further fractional distillation.

Upon distilling the purified residuum from the crude petroleum at higher temperatures, "paraffin oils" are obtained together with a residue of pitch. These paraffin oils are filtered while hot through freshly burned boneblack, for the purpose of removing odor and color, and then subjected to distillation until the desired consistence or melting-point of the residuary portion is obtained. The official varieties differ from each other simply in the graded removal of lower hydrocarbons.

Paraffin and petrolatum are not saponifiable and not subject to rancidity. If properly purified they consist only of hydrocarbons, which are not affected at all by cold acids and alkalies, and only slightly by hot acids; hence the name paraffins has been given to the products, from the words *parum*, too little, and *affinis*, allied, on account of their lack of affinity for other substances.

Hard paraffin is obtained partly as a residue from the above-mentioned paraffin oils and also largely by the purification with sulphuric acid, etc., of ozokerite or mineral (earth) wax. It occurs as a white, crystalline, odorless, wax-like body, having a melting-point varying from 50° to 80° C. (122°–174° F.), according to its source. Ceresin is a yellow variety of purified earth wax, often used to adulterate yellow beeswax.

Petroleum Benzin.—This product, also known as petroleum ether, and commercially simply designated as benzin, is a mixture of hydrocarbons, chiefly pentane, C_5H_{12}, and hexane, C_6H_{14}. The official article constitutes that fraction of purified petroleum distilling between 45° and 60° C. (113° and 140° F.), as indicated by the boiling-point given in the Pharmacopœia, and should have a specific gravity of 0.638–0.660 at 25° C. (77° F.). It is insoluble in water, soluble in about 6 parts of alcohol, and readily soluble in ether, chloroform, volatile oils and in fixed oils with the exception of castor oil. It is highly inflammable and its vapor when mixed with air and ignited explodes violently; hence it should be carefully preserved in tin cans or well-stoppered bottles in a cool place remote from lights or fire.

Purified Petroleum Benzin.—Commercial benzin is not suitable for pharmaceutical purposes, and the Pharmacopœia therefore directs its purification as follows: Petroleum benzin is first mixed with an acid solution of potassium permanganate, and the mixture set aside for 24 hours with frequent agitation; after decantation of the lighter fluid this is treated for several hours with an alkaline solution of potassium permanganate, again bringing the two fluids into intimate contact by frequent agitation. The benzin thus purified is decanted and washed several times with plain water, after which it is again decanted and should then be free from sulphur compounds and other impurities.

CHAPTER LVIII.

VOLATILE OILS AND RESINS.

VOLATILE oils form a very important class of pharmaceutical plant products. Their physical properties and the mode of obtaining them have already been fully considered on pages 209–221. Chemically, volatile oils differ radically from fats and fixed oils, as they are not capable of saponification and contain no glycerin. Moreover, by exposure to air, they do not become rancid, but many undergo resinification. They may be said to consist of hydrocarbons of the aromatic series, usually associated with oxygen derivatives, alcohols, aldehydes, compound ethers, acids, ketones, and phenols. While some volatile oils are complex mixtures, others are of very simple composition. The hydrocarbons found in volatile oils all belong to one of the following groups: terpenes of the composition $C_{10}H_{16}$, sesquiterpenes of the composition $C_{15}H_{24}$, diterpenes of the composition $C_{20}H_{32}$, and polyterpenes of the composition $(C_{10}H_{16})_x$. The terpenes include dextrorotatory pinene, found in American oil of turpentine; lævorotatory pinene, found in French oil of turpentine; camphene, a solid body, melting at 48°–49° C. (118.4°–120.2° F.), and found in the oils of camphor, citronella, lemon, and others; dextrorotatory limonene (known also as hesperidine, citrene, and carvene), constituting the bulk of the oils of orange peel, lemon, and erigeron, and about 50 per cent. of oil of caraway; lævorotatory limonene, constituting about 50 per cent. of American oil of spearmint; optically inactive limonene, usually designated as dipentene; sylvestrene, found in Swedish and Russian oil of turpentine; phellandrene, of which the dextrorotatory variety is found in oil of water fennel, and the lævorotatory variety forms an objectionable constituent of the oils of eucalyptus; of these pinene and limonene are very widely distributed in nature. Although terpenes frequently form the bulk of volatile oils, they may in some instances be considered, from the standpoint of flavor and medicinal properties at least, merely as diluents for the more important constituents, and, on account of their sparing solubility in mixtures of alcohol and water, are frequently removed. Oils thus deprived of their hydrocarbon constituents are known as terpeneless oils, and have been largely offered for sale for a number of years, especially for the manufacture of liquors, essences, and spirits. The group of sesquiterpenes includes cadinene, caryophyllene, cedrene, humulene, and santalene. Other hydrocarbons met with are cymene, myrcene, sabinene, styrene, thujene, etc.

Among the alcohols found in volatile oils, both free and in the form of esters, are allyl, amyl, butyl, methyl and terpin alcohol, borneol, geraniol, linalool, menthol, sabinol, santalol and terpineol. The aldehydes comprise benzoic and cinnamic aldehydes, citral, and citronellal; the ketones, camphor, carvone, and menthone; the phenols and phenolic ethers, carvacrol, chavicol, eugenol, safrol, and thymol. Besides acetic, anisic, benzoic, butyric, formic, salicylic, and valeric acids, sulphocyanic and hydrocyanic acids are also present in some oils; with the exception of hydrocyanic acid they are usually in combination as esters, and but rarely present in the free state.

The behavior of volatile oils with acids, alkalies, and other reagents must naturally vary greatly, owing to the diversity in their constitution. Those oils composed almost wholly of terpenes form either solid or liquid compounds with hydrochloric acid. Other oils are oxidized and converted into resin-like bodies by nitric acid, while sulphuric acid thickens some volatile oils and completely chars others. Color reactions also occur between some of the oils and sulphuric and other acids. Alkali carbonates are without much effect on volatile oils unless the latter contain acids, but alkali hydroxides, in both aqueous and alcoholic solution, are more active, removing phenols, saponifying compound ethers, etc. Acid alkali sulphites, when added to volatile oils containing aldehydes, combine with the latter to form crystalline compounds. Iodine reacts violently with some oils, and bromine forms crystallizable tetrabromides with others.

For the examination of volatile oils both chemical and physical methods are employed; of the former, determination of alcohols, aldehydes, esters, phenols, etc., are important, while of the latter the determination of specific gravity, optical rotation, congealing-point, and solubility in alcohol, offers valuable information for deciding upon the true character of the oil.

The specific gravity of volatile oils may be ascertained by means of the Mohr-Westphal balance (see page 55), or a small pycnometer. For the determination of the specific rotation of oils, which is now required in many cases, the necessary explanation may be found on pages 580 and 581 of the Pharmacopœia. The degree of solubility in alcohol is at times useful for detection of certain adulterants, such as oil of turpentine, rectified petroleum, and fatty oils; it is best determined by placing 1 Cc. of the oil in a small cylinder of 10 Cc. capacity, and graduated into $\frac{1}{2}$'s or $\frac{1}{10}$'s, and adding small portions of 90, 80, or 70 per cent. alcohol, as the test may require, until, after vigorous agitation, a perfectly clear solution results, free from turbidity and separation. As determination of the congealing-point is required for only two of the official oils, the method will be given under the respective oils.

The following analytical methods in use among chemists give an idea as to the mode of determining quantitatively some of the chief constituents of volatile oils.

Determination of esters, such as are found in the oils of bergamot, lavender, orange flowers, peppermint, and wintergreen: Place 2 Gm. of the oil into a suitable 100 Cc. flask provided with a sound cork and a reflux condenser; in place of the condenser, a glass tube thirty-six or forty inches long may be used. Add 20 Cc. of $\frac{N}{2}$ alcoholic potassium hydroxide solution to the oil and heat the mixture to boiling on a water-bath for one hour. When cool dilute the contents of the flask with about 50 Cc. of distilled water and titrate the excess of alkali by means of $\frac{N}{2}$ sulphuric acid. From the number of cubic centimeters of $\frac{N}{2}$ KOH solution thus ascertained as having been required for saponification of the ester in the oil calculate the number of milligrammes of KOH required (1 Cc. $\frac{N}{2}$ KOH sol. = 0.02787 Gm. KOH) for 1 Gm. of the oil, and from this find the percentange of ester originally present. Every milligramme of KOH required for 1 Gm. of the oil represents 0.35 (0.349 +) per cent. of acetate of alcohols of the composition $C_{10}H_{17}OH$, or 0.353 (0.3528 +) per cent. of acetate of alcohols of the composition $C_{10}H_{19}OH$, as shown by the following proportions:

$$\overset{KOH}{55.74} : \overset{C_{10}H_{17}C_2H_3O_2}{194.68} :: \overset{KOH}{0.001} : \overset{C_{10}H_{17}C_2H_3O_2}{x} \qquad x = 0.00349 +.$$

$$\overset{KOH}{55.74} : \overset{C_{10}H_{19}C_2H_3O_2}{196.68} :: \overset{KOH}{0.001} ; \overset{C_{10}H_{19}C_2H_3O_2}{x} \qquad x = 0.003528 +.$$

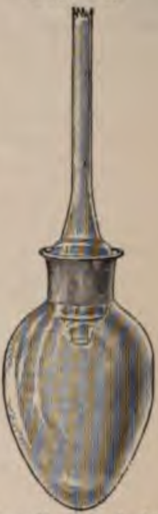
If, therefore, 2 Gm. of oil of lavender were found to require 0.194 Gm. of KOH, the oil must contain 33.95 per cent. of $C_{10}H_{17}C_2H_3O_2$, for $194 \times 0.0035 = 0.6790$ and 0.6790×50 (or $\frac{0.6790 \times 100}{2}$) = 33.95.

The figures in the above calculations refer to the presence of esters as acetates only; when benzoates, salicylates, or other esters are present, or a possible mixture of these with acetate, the results may be reported either as equivalent to so much acetate or different calculations made for other esters if they alone be present.

Determination of alcohols: Since the different alcohols met with in volatile oils are rarely, if ever, present wholly in an uncombined state, it becomes necessary to determine, first, the amount in combination as esters and then the total amount present, and, lastly, find the amount of uncombined alcohol by difference. Having saponified a given weight of the oil by the method above explained, the percentage of alcohol present as an ester can be readily calculated by multiplying the number of cubic centimeters of $\frac{N}{2}$ KOH solution required for saponification by 0.07649 for alcohols having the composition $C_{10}H_{17}OH$, or by 0.07749 for alcohols belonging to the $C_{10}H_{19}OH$ group, then dividing the product by the weight of oil used and multiplying the quotient by 100. The next step is to convert the uncombined alcohol into an ester, which is done by acetylization. Into a suitable flask, provided with a reflux condenser ground into the neck, as shown in Fig. 301, are put 10 Gm. of the oil, an equal volume of acetic anhydride $(C_2H_3O)_2O$, and

1 Gm. of dry sodium acetate; the mixture is then boiled for an hour and cooled. The product is transferred to a separator, and washed well with water, then with a dilute solution of sodium hydroxide, and, again, with water until the reaction is neutral, and is finally dried with anhydrous calcium chloride or sodium sulphate. 2 Gm. of the dry acetylized oil are transferred to a suitable flask, using a small quantity of 95 per cent. ethyl alcohol to transfer the last portions, and saponified with 20 Cc. of normal alcoholic potassium hydroxide solution in the manner explained in the preceding paragraph, except that normal sulphuric acid must be used in this case to titrate the excess of alkali. If the number of Cc. of normal alkali required by the oil be now multiplied by 0.15298 or 0.15498 the total amount of alcohol present in the 2 Gm. of oil used will be found, and multiplying this product by 50 gives the percentage. The difference between this percentage and that of alcohol found in combination represents the uncombined alcohol.

FIG. 301.



Acetylization flask.

The method is well adapted for the quantitative determination of borneol, geraniol, and menthol, but does not give satisfactory results with linalool and terpineol; the reaction occurring may be illustrated by the following equation: $C_{10}H_{17}OH + (C_2H_3O)_2O = C_{10}H_{17}C_2H_3O_2 + HC_2H_3O_2$. If aldehydes are also present in the oil the acetylization method cannot be used.

Determination of aldehydes: The well-known property of aldehydes of forming water-soluble addition-compounds with acid sodium sulphite is made use of in determining the aldehyde content of volatile oils quantitatively. Cinnamic aldehyde in oil of cassia cinnamon, and citral in oil of lemongrass, can both be determined very satisfactorily by the following method, which is based on the observation that when either oil is shaken for some time with hot acid sodium sulphite solution the decrease in volume of the oil corresponds about to the proportion of aldehyde present. For this purpose use is made of a special flask of about 100 Cc. capacity with a long, narrow neck (13 x 8 Cm.), which is graduated into tenths of a cubic centimeter. (See Fig. 302.) Exactly 10 Cc. of the oil are put into the flask by means of a pipette, and a like volume of a warm 30 per cent. solution of acid sodium sulphite is added. The flask is placed in a boiling water-bath, and more of the acid sulphite solution is gradually added until a uniform fluid is obtained, filling the flask nearly three-fourths. When all solid particles, at first formed, have disappeared and the characteristic odor of the respective aldehyde is no longer discernible, the flask is filled with acid sulphite solution up to the zero point of the graduated scale.

perature reached during the crystallization is regarded as the congealing-point.

Oil of Betula.—This oil, also known as oil of sweet birch, constitutes probably the bulk of the commercial oil of wintergreen. Investigations made by Power and Kleber (1895) have shown that oil of sweet birch, in its unrectified state, contains about 99.8 per cent. of methyl salicylate, together with a very small amount of a paraffin triacontan, $C_{30}H_{62}$, an aldehyde or ketone, and the ester, $C_{14}H_{24}O_2$; it does not, however, contain the alcohol $C_8H_{16}O$, found in oil of gaultheria. It does not exist ready-formed in the bark of the tree, which latter is devoid of odor, but is the result of a reaction between the glucoside gaultherin, $C_{14}H_{18}O_8$, and a peculiar ferment in the presence of water; maceration of the crushed bark is allowed to go on for twelve hours before distillation of the mixture is begun. The hydrolysis of the glucoside may be represented by the following equation: $C_{14}H_{18}O_8$ (gaultherin) $+$ H_2O $=$ $C_6H_4(OH)COOCH_3$ (methyl salicylate) $+$ $C_6H_{12}O_6$ (dextrose).

Oil of betula, when carefully rectified, is colorless, but the commercial oil frequently has a reddish color, due to contact with metal. It is optically inactive and in this respect differs slightly from true oil of wintergreen, especially when the latter is fresh. The specific gravity of oil of sweet birch is identical with that of the natural oil of wintergreen, and, like the latter, the oil forms a clear solution with five times its volume of 70 per cent. alcohol at a temperature of 20°–25° C. (68°–77° F.).

Empyreumatic oil of birch, known commercially as *oleum rusci* and also as *oleum betulinum* or *oleum muscoviticum*, is obtained by distillation of birch tar or *daggett*, derived by destructive distillation from the wood of the common European birch, betula alba. The oil is of a dark, brown-red color, having a peculiar penetrating odor like that of Russia leather, and somewhat resembles oil of cade in its medicinal properties.

Oil of Bitter Almond.—The oil to which this name is applied need not necessarily be obtained from bitter almonds, the Pharmacopœia recognizing also the volatile oil produced from other seeds containing the glucoside amygdalin, provided the oil conforms to the official requirements of not less than 85 per cent. of benzaldehyde, and not less than 2, nor more than 4, per cent. of hydrocyanic acid. The oil does not pre-exist in the seed, but is produced from amygdalin by fermentation set up in the presence of water, as shown by the equation $C_{20}H_{27}NO_{11}$ (amygdalin) $+ 2H_2O = C_6H_5COH$ (benzoic aldehyde or benzaldehyde) $+$ HCN (hydrocyanic acid) $+ 2C_6H_{12}O_6$ (dextrose). Previous to the distillation of the volatile oil, the seeds must be deprived of their fatty oil by powerful pressure applied to the crushed seed, the presscake being subsequently ground to fine powder and mixed with 6 or 8 parts of warm water, not above 50°

or 60° C. (122°–140° F.), and allowed to stand for about twelve hours, so that the reaction may be completed, after which the oil formed is distilled with steam by passing the same through the mixture.

Oil of bitter almond is optically inactive. It is soluble in 300 parts of water and in an equal volume of 70 per cent. alcohol. Its chief constituent, as stated above, is benzoic aldehyde, the percentage present being determined exactly in the same manner as directed for the official benzaldehyde, see page 699, 12 drops of the oil being used for each assay. In the official assay for hydrocyanic acid content, all the acid present is precipitated by $\frac{N}{10}$ $AgNO_3$ solution, potassium chromate being used as indicator. Each Cc. of the silver solution corresponding to 0.002684 Gm. of HCN, not less than 7.45 nor more than 15 Cc. will be required to show that the amount of acid is within the limits demanded by the Pharmacopœia, provided 1 Gm. of oil be used for the assay.

Considerable synthetic oil of bitter almond is offered for sale, which is made from toluene, and is recognized in the Pharmacopœia as Benzaldehyde. This contains no hydrocyanic acid, but, if imperfectly purified, may contain chlorinated by-products, and hence the Pharmacopœia gives special tests to indicate their absence in oil of bitter almond. At one time nitrobenzene was offered as artificial oil of bitter almond, on account of its resemblance in odor to the true oil. This compound, also commercially known as *essence or oil of mirbane*, may be detected by its insolubility in diluted alcohol. The presence of other volatile oils may be ascertained by treatment with acid sodium sulphite solution, whereby an addition compound of benzaldehyde is formed, $C_6H_5COH.NaHSO_3$, which goes into solution upon application of heat, and may thus be removed, leaving other oils floating on the surface.

Exposed to the air, oil of bitter almond slowly undergoes oxidation, especially in half-filled bottles, the benzoic aldehyde being converted into benzoic acid, C_6H_5COOH. Crystals of the acid are sometimes seen in old oil, and when thus contaminated the oil should not be used.

Oil of Cade.—This oil, obtained by destructive distillation of the wood of the prickly cedar, a species of juniper indigenous to the southern part of France, is also known as *empyreumatic oil of juniper*, and consists of sesquiterpene, cadinene, $C_{15}H_{24}$, and a mixture of undetermined phenols.

Oil of Cajuput.—The constituents are a neutral body, cineol or eucalyptol, $C_{10}H_{18}O$ (about 67 per cent.), an alcohol, terpineol, $C_{10}H_{17}OH$, some pinene and undetermined terpenes.

Although the chief constituent of oil of cajuput is optically inactive, the oil is slightly lævogyrate, to the extent of about 2 degrees, owing to the invariable presence of lævorotatory pinene. The Pharmacopœia demands the absence of copper, as shown by the test with potassium ferrocyanide, and demands the presence of not less than 55 per cent. of cineol, to be determined as follows: 10 Cc. of the oil dissolved in 50 Cc. of purified petroleum benzin are poured into a beaker, which is immersed in a freezing mixture; phosphoric acid is then added, drop by drop, with constant stirring, until the white mass of cineol phosphate formed begins to assume a yellowish or pinkish tint; the magma is then transferred to a force filter, washed with cold purified petroleum benzin, and dried by pressure between two porous plates. The precipitate, cineol phosphate, is transferred to a narrow graduated cylinder, warm water is added, and the oily liquid, cineol, which separates is measured. The number of Cc. of cineol thus obtained, when multiplied by 10, will represent the percentage of cineol present in the oil.

Oil of Caraway.—This oil is composed of a terpene, limonene, $C_{10}H_{16}$, and a ketone, carvone, $C_{10}H_{14}O$, formerly known as carvol; both compounds are dextrorotatory and are present in proportions varying from 35 to 50 of the former to 65 to 50 of the latter.

Carvone is the important constituent of oil of caraway, and is the substance recognized in the German Pharmacopœia under the Latin title Oleum Carvi. The angle of rotation of the oil varies from $+70°$ to $+80°$, and since it is $+62.5°$ for pure carvone and $+125°$ for pure limonene, it is evident that the rotatory power of the oil will increase with a diminished carvone content. The Pharmacopœia does not give a method of assay for oil of caraway, but the following method of Kremers and Schreiner for determination of the carvone present, by conversion into carvoxime, $C_{10}H_{14}N.OH$, has been found satisfactory:

To a solution of 10 Gm. of oil, dissolved in 25 Cc. of alcohol, 5 Gm. of hydroxylamine hydrochloride and 6.5 Gm. of sodium bicarbonate are added. This mixture is boiled on a water-bath for half an hour in a flask connected with a reflux condenser, 25 Cc. of water are then added, and the alcohol is distilled off on the water-bath. Steam is then passed through the liquid until traces of carvoxime come over. The last portions of the distillate are collected separately in test-tubes, and when traces of crystals of carvoxime appear on the surface the operation is interrupted. The tube of the condenser is washed with a little hot water, and this, as well as the last-collected distillate, containing some carvoxime, is returned to the flask. The contents of the flask are allowed to cool, and after the carvoxime has completely solidified, it is removed from the sides of the flask by means of a loop of stiff wire, thrown upon a force filter, washed, and dried by suction. The air-dried carvoxime is transferred to a tared glass dish and heated for one hour on a water-bath, and when cool weighed. To the weight thus obtained 0.100 Gm. is added, as this is about the quantity lost during heating. From the weight of the carvoxime that of the carvone may be readily calculated, 164.67 parts of the former corresponding to 149.66 parts of the latter, or the weight of carvoxime obtained, expressed in Gm., when multiplied by 0.9088, gives the weight of the equivalent amount of carvone.

Oil of Chenopodium.—This oil, also known as oil of wormseed, has been found to contain a terpene, most likely pinene, and an oxidized body, $C_{10}H_{16}O$, not as yet further investigated. It should be soluble in five times its volume of 70 per cent. alcohol, the Pharmacopœia also requiring that its angle of rotation shall not be greater than —5 degrees at 25° C. (77° F.) in a 100 Mm. tube. Nearly all oil of chenopodium is distilled in Maryland and is usually marketed as Baltimore oil of wormseed.

Oil of Cinnamon.—Ordinary oil of Chinese cinnamon, usually designated as *oil of cassia*, is the kind recognized in the U. S. and German Pharmacopœias, whereas the British Pharmacopœia recognizes the oil of Ceylon cinnamon. It consists chiefly of cinnamic aldehyde, C_8H_7COH, with some cinnamyl acetate, $C_9H_9C_2H_3O_2$, and small amounts of cinnamic acid, $C_9H_8O_2$, or $C_6H_5CHCHCOOH$. The value of this oil, which is subject to adulteration, depends upon the amount of cinnamic aldehyde present, of which it should contain at least 75 per cent. by volume, and which may be determined with acid sodium sulphite, as explained on page 683. The chemical reactions involved in the official assay process may be shown by the following equations, an insoluble aldehyde addition-compound being first formed, to which the name sodium cinnamalhydroxysulphonate has been given; this when boiled with water breaks up into cinnamic aldehyde and sodium sulphocinnamalhydroxysulphonate, thus: $C_8H_7COH + NaHSO_3 = C_8H_7COH.NaHSO_3$; $2C_8H_7COH.NaHSO_3 = C_8H_7COH + C_6H_5CH_2CH(SO_3Na).COH.NaHSO_3$. In order to convert all of the aldehyde present into the second compound soluble in water, an excess of acid sodium sulphite must be added.

A characteristic reaction of oil of cinnamon is the formation of a crystalline compound with nitric acid when equal volumes of the oil and acid are mixed at 0° C. (32° F.); the product is an addition-compound of cinnamic aldehyde and nitric acid, $C_8H_7COHHNO_3$. Oil of Ceylon cinnamon, which has a finer aroma than the official oil, contains, besides cinnamic aldehyde, some eugenol and phellandrene.

Oil of Cloves.—The chief constituent of this oil is eugenol, $C_6H_3.C_3H_5.OCH_3.OH$, a monatomic phenol, which is present in prime oil to the extent of from 75 to 85 per cent. and over; besides this, the oil also contains a sesquiterpene, $C_{15}H_{24}$, called caryophyllene, and about 2 or 3 per cent. of eugenol acetate. The reaction with potasssium hydroxide or ammonia, mentioned in the Pharmacopœia, depends upon the formation of potassium or ammonium eugenol, $C_6H_3C_3H_5OCH_3OK$ or $C_6H_3C_3H_5OCH_3ONH_4$.

The value of oil of cloves lies wholly in the eugenol present, of which the Pharmacopœia requires not less than 80 per cent. to be present. The simplest method for determining the eugenol-content of oil of cloves is that of shaking 10 Cc. of the oil with 100 Cc. of official potassium hydroxide solution for five minutes in a suitably graduated flask (see Fig. 302, page 684); then allow the liquids to separate, adding sufficient alkali solution to raise the lower limit of the oily layer to the zero point of the graduated scale, and note the volume of oil remaining, which substracted from 10 indicates the number of Cc. of eugenol dissolved by the alkali solution, and multiply the remainder by 10 to find the percentage of phenol in the sample of oil. This method, while easily applied, is not absolutely accurate, as already explained on page 684, but should always be used when an oil appears at all suspicious, in view of the fact that oil of cloves is sometimes met with from which a portion of the eugenol has been abstracted. A more accurate determination of eugenol in oil of cloves is to convert it into crystalline benzoyl eugenol, $C_{10}H_{11}OC_6H_5CO$, by means of benzoyl chloride, and to calculate from the weight of the crystalline compound formed the percentage of eugenol in the oil. The method is given in the *American Journal of Pharmacy* for 1892, page 508.

Oil of Copaiba.—This oil consists chiefly of a sesquiterpene, $C_{15}H_{24}$, identical with that found in cloves and known as caryophyllene. It is readily oxidized by exposure to air and gradually thickens. It is lævogyrate, the angle of rotation varying from −7 to −35°.

Oil of Coriander.—The oil consists of about 90 per cent. of linalool and about 6 per cent. of pinene, together with some unknown substance, to which the peculiar aroma is due. It is soluble in 3 volumes of 70 per cent. alcohol and in all proportions of 80 and 90 per cent. alcohol. Oil of coriander is dextrogyrate, its angle of rotation varying from 7° to 14°.

Oil of Cubeb.—The composition of this oil varies somewhat with age. Recent oil, distilled from fresh fruit, consists chiefly of a sesquiterpene, cadinene, $C_{15}H_{24}$, with some dipentene, $C_{10}H_{16}$, but if old or obtained from old fruit, cubeb camphor, $C_{15}H_{24}.H_2O$, is also present. The oil is lævogyrate, the angle of rotation varying from −25° to −40°.

Oil of Erigeron.—This oil is better known as oil of fleabane, and consists chiefly of dextrorotatory limonene, $C_{10}H_{16}$, together with an undetermined substance readily decomposed by heat. Upon exposure to air the oil rapidly thickens and assumes a darker color. The presence of oil of fireweed and oil of turpentine may be readily detected by not yielding a clear solution with an equal volume of 94 per cent. of alcohol. Oil of erigeron is dextrogyrate, the angle of rotation being about 50°.

Oil of Eucalyptus.—The composition of this oil depends largely on its source. The oils of Eucalyptus globulus and Eucalyptus oleosa consist chiefly of cineol, which in the case of eucalyptus oils is generally called eucalyptol and to which they owe their medicinal and antiseptic value; the former oil contains also some pinene and a ketone, $C_{10}H_{16}O$, called eudesmol, while the latter oil, in place of eudesmol, contains a sesquiterpene and an aldehyde, $C_{10}H_{13}$ COH, known as aromadendral and resembling cumin aldehyde in odor. The less valuable oils of eucalyptus contain less cineol, but pinene and varying amounts of phellandrene. The test for the presence of excessive quantities of phellandrene in oil of eucalyptus depends upon the formation of crystalline phellandrene nitrite and can be made more delicate, according to Power, by mixing the oil first with 5 Cc. of petroleum benzin, then adding the sodium nitrite solution and lastly the glacial acetic acid, drop by drop.

The Pharmacopœia demands that oil of eucalyptus shall contain not less than 50 per cent. of cineol, which is determined by conversion into cineol phosphate exactly as stated under Oil of Cajuput. The oil is somewhat dextrogyrate, but the angle of rotation should not be greater than 10°. Cineol being inactive optically, the greater the cineol-content the lower the angle of rotation.

Some eucalyptus oils contain also citral, $C_{10}H_{16}O$, citronellal, $C_{10}H_{18}O$, and geraniol, $C_{10}H_{17}OH$.

Oil of Fennel.—This oil contains the terpenes, pinene, phellandrene, and dipentene, together with fenchone, $C_{10}H_{16}O$, and anethol, $C_{10}H_{12}O$; the latter is usually present to the extent of more than 50 per cent. and separates in crystals upon a reduction of the temperature, hence the higher the temperature at which this occurs the better the oil. The Pharmacopœia has fixed the congealing-point at not below 5° C. (41° F.) to be determined as follows: Transfer about 10 Cc. of the oil to a test-tube placed in a freezing mixture; insert a thermometer at once into the oil, and allow it to remain undisturbed until the temperature has fallen to about —5° C. (23° F.). Induce crystallization either by scratching the inner-wall of the test-tube with the thermometer or by the addition of a particle of solid anethol, and stir continuously during the solidification of the oil. The highest temperature reached during the crystallization is regarded as the congealing-point.

Oil of fennel is dextrogyrate, its angle of rotation varying from 12° to 24°, which, together with the higher congealing-point of oil of anise, readily distinguishes the two oils from each other.

Oil of Gaultheria.—The true oil contains, according to Power and Kleber, 1895, about 99 per cent. of methyl salicylate together with a small amount of paraffin, probably triacontan, $C_{30}H_{62}$, an aldehyde or ketone, an apparently secondary alcohol, $C_8H_{16}O$, and an ester, $C_{14}H_{24}O_2$, formed by this alcohol and an acid, $C_6H_{10}O_2$, which latter is the result of oxidation of the aldehyde previously mentioned. The alcohol and the ester are said to possess the very penetrating odor characteristic of true oil of gaultheria. Although some of the oil is no doubt formed in the leaves, by far the larger portion obtained by distillation is the result of the hydrolysis of the glucoside gaultherin, as already explained under Oil of Betula on page 686, thus resembling oil of sweet birch very closely in composition. It has a specific gravity of from 1.180 to 1.187 at 15° C. (59° F.), and yields a clear solution when mixed with five times its volume of 70 per cent. alcohol at a temperature of from 20° to 25° C. (68°–77° F.). Neither oil of gaultheria nor oil of sweet birch contains any trace of benzoic acid or its esters, nor does either oil contain any terpene or sesquiterpene, as was at one time supposed.

There is little doubt that commercially the oils of betula and of gaultheria are considered identical and sold indiscriminately under the name oil of wintergreen.

Oil of Hedeoma.—According to Kremers, this oil contains pulegone, $C_{10}H_{16}O$, and two ketones of the composition $C_{10}H_{18}O$, which are looked upon as reduction-products of the former body. Formic and acetic acids are also present. It forms a clear solution with 2 volumes of 70 per cent. alcohol, by which test the presence of oil of turpentine and rectified petroleum may be quickly detected. Commercially this oil is known as oil of pennyroyal.

Oil of Juniper.—The chief constituent is pinene, with some cadinene, $C_{15}H_{24}$, and a body, as yet undetermined, to which the peculiar odor and taste of the oil are due. The oil obtained from the fruit only should be used in pharmacy.

Oil of Lavender Flowers.—Two varieties of this oil, English and French, are found on the market, the former being usually designated as oil of garden lavender, because distilled from cultivated plants. English oil of lavender contains about 5–10 per cent. of linalyl acetate, $C_{10}H_{17}C_2H_3O_2$, and some free linalool; also considerable cineol. The French oil contains from 30–40 per cent. of linalyl acetate, free linalool and geraniol, besides small amounts of pinene and traces of cineol. Both oils are lævogyrate, the angle of rotation not exceeding —10°, and form clear solutions with 3 parts of 70 per cent. alcohol.

The percentage of ester, linalyl acetate, present in any sample of oil of lavender may be determined by the general method of saponification with alcoholic solution of potassium hydroxide, as explained on page 682.

Oil of Lemon.—Quantitatively, the chief constituent of oil of lemon is dextrorotatory limonene, but an aldehyde known as citral, $C_9H_{15}COH$, is of much greater importance, although rarely present to the extent of more than 6 or 8 per cent. Other constituents of the oil are pinene, phellandrene, citronellal, geranyl acetate, etc. The most dangerous adulteration of oil of lemon is perhaps oil of lemon previously deprived of its aldehyde, and hence an assay of the citral content should be made whenever suspicion is aroused in connection with any sample of the oil. The Pharmacopœia demands the presence of not less than 4 per cent. of citral, to be determined in a manner practically identical with the assay of benzaldehyde in oil of bitter almond, which see under Benzaldehyde, on page 699.

The sodium sulphite solution used in the official test shows an alkaline reaction toward phenolphthalein, whereas acid sodium sulphite, formed after addition of a little hydrochloric acid, shows a neutral reaction. When the acid sodium sulphite thus formed has reacted with the aldehyde citral producing the sparingly soluble addition-compound, $C_9H_{15}.CH\ (OH)\ SO_3Na$, alkaline reaction is again observed, which is overcome by the further addition of hydrochloric acid until, finally, when all the citral has been taken up, a neutral reaction will remain. In the presence of an excess of acid sodium sulphite, the sparingly soluble compound above mentioned is converted into a soluble compound, $C_9H_{17}.(SO_3Na)_2.COH$, to which the name sodium citraldihydrosulphonate has been given. In order to produce the soluble compound, 2 molecules of acid sodium sulphite are required for each 1 of citral, which in turn require 2 molecules of hydrochloric acid for their formation from the normal sodium sulphite used. 150.98 Gm. of citral will therefore require 72.36 Gm. of absolute hydrochloric acid, as shown by the following equation: $2Na_2SO_3 + 2HCl + C_9H_{15}COH = C_9H_{17}.(SO_3Na)_2.COH + 2NaCl$; hence, as 72.36 Gm. of hydrochloric acid are contained in 4000 Cc. of the $\frac{N}{2}$ acid, each Cc., containing 0.01809 Gm. of HCl, will correspond to 0.037745 Gm. of citral.

Oil of Mustard, Volatile.—Like oil of bitter almond, this oil does not pre-exist in the plant; it is obtained by macerating crushed black mustard seed, after the removal of fixed oil by expression, with water, when a reaction sets in between sinigrin, a glucoside, and myrosin, an albuminoid body. Sinigrin is, chemically, potassium myronate, $C_{10}H_{18}NS_2KO_{10}$, which, under the influence of the albuminoid ferment, is split up into allyl isosulphocyanate, acid potassium sulphate, and dextrose, thus: $C_{10}H_{18}NS_2KO_{10} = C_3H_5NCS$ (volatile oil of mustard) $+ KHSO_4 + C_6H_{12}O_6$. Since the albuminoid myrosin is rendered inert at a temperature between 60° and 70° C. (140° and 158° F.), mustard which has been heated to this point will not yield the volatile oil, nor can hot water be employed in its manufacture; for the same reason, mustard plasters should never be dipped into water that is more than lukewarm.

Volatile oil of mustard always contains traces of carbon disulphide. It has been prepared synthetically by decomposing allyl iodide, C_3H_5I, by means of potassium sulphocyanate in alcoholic solution.

White mustard seed does not yield volatile oil of mustard, since it does not contain sinigrin, but, instead, sinalbin, having the composition $C_{30}H_{44}N_2S_2O_{16}$. When sinalbin reacts with myrosin in the presence of water, a very active, oily but non-volatile principle, to which the name acrinyl sulphocyanate, $C_7H_7O.CSN$, has been given, is formed, together with acid sinapine sulphate, $(C_{16}H_{23}NO_5)H_2SO_4$, and glucose, $C_6H_{12}O_6$.

The official method of valuation depends upon the formation of thiosinamine by the action of ammonia on allyl isosulphocyanate, thus, $C_3H_5NCS + NH_3 = C_3H_5CSN_2H_3$; this is acted upon by the silver nitrate, or rather silver in the form of oxide held in solution by the ammonia, whereby the sulphur is removed and a new compound, allylcyanamide, $CN.NH.C_3H_5$, is produced. As each molecule of thiosinamine, representing 1 molecule or 98.4 parts of allyl isosulphocyanate, requires 2 molecules or 337.38 parts of silver nitrate for complete removal of the sulphur present, each Cc. of the silver solution containing 0.016869 Gm. of silver nitrate corresponds to 0.00492 Gm. of allyl isosulphocyanate; the excess of silver solution is determined by titration with potassium sulphocyanate solution. In the official test only 0.1 Gm. of oil of mustard is used for the assay, and the excess of silver nitrate solution determined in one-half of the filtrate, representing 0.05 Gm. of oil; hence to indicate 92 per cent. of allyl isosulphocyanate, as demanded by the Pharmacopœia, should require not more than 5.6 Cc. of $\frac{N}{10}$ potassium sulphocyanate solution, showing that 9.4 Cc. of the silver solution have been used up by 0.05 Gm. of the oil, for 92 per cent. of $0.05 = 0.046$ and $0.046 \div 0.00492 = 9.35$.

Oil of Nutmeg.—The Pharmacopœia recognizes only the volatile oil obtained from the seed of nutmeg as oil of myristica, whereas in Germany the oil distilled from mace, the arillus of the nutmeg, is officially named as ethereal oil of nutmeg. The two oils resemble each other closely in physical properties and chemical composition, although the oil obtained from the seed contains a larger proportion of terpenes than oil of mace, and is more decidedly dextrogyrate, its angle of rotation ranging from 14° to 28°. The chemical constituents of both oils are pinene, dipentene, myristicol $C_{10}H_{16}O$, myristicin $C_{12}H_{14}O_3$, and some myristinic acid.

The expressed or fatty oil of nutmeg, containing about 6 per cent. of volatile oil, is recognized in the German Pharmacopœia as Oleum Nucistæ, although the official German title is oil of nutmeg. It is better known as nutmeg butter.

Oil of Orange Peel.—The official oil of orange is that obtained by expression only from the rind of the sweet orange, since some of the constituents upon which the odor of the oil depends are destroyed in part by distillation. Oil of orange contains about 90 per cent. of dextrorotatory limonene, together with the aldehydes citral and citronellal, and some methyl anthranilate, $CH_3C_9H_6NO_2$. It is strongly dextrogyrate, not less than 95° in a 100 Mm. tube at 25°C. (77° F.). The presence of oil of turpentine may be detected, as recommended by the Pharmacopœia, by the formation of nitroso-pinene and pinene nitrosochloride in that fraction of the oil distilling below 170° C. (338° F.).

Oil of orange, like oil of lemon, when carelessly exposed to air and light, gradually assumes a terebinthinate odor, which can be prevented by addition of 5 or 10 per cent. of pure alcohol.

Oil of bitter orange, also offered for sale, closely resembles that obtained from the sweet orange, but is not officially recognized.

Oil of Peppermint.—There is probably no volatile oil used in pharmacy of which a greater variety is offered for sale; besides five or six different brands of American oil, oils distilled from English, German, and Japanese peppermint herb are also on the market. Oil of peppermint shows a greater complexity in composition than any other volatile oil known, an analysis in 1894 by Power and Kleber of the average American oil having developed the following constituents, fifteen in number: Acetaldehyde, C_2H_4O; acetic acid, $HC_2H_3O_2$; iso-valeraldehyde, $C_5H_{10}O$; iso-valeric acid, $HC_5H_{10}O_2$; three isomeric terpenes, pinene, phellandrene, and limonene, $C_{10}H_{16}$; cineol or eucalyptol, $C_{10}H_{18}O$; menthone—a ketone—$C_{10}H_{18}O$; menthol, $C_{10}H_{19}OH$; two compound ethers, menthyl acetate, $C_{10}H_{19}C_2H_3O_2$, and menthyl iso-valerate, $C_{10}H_{19}C_5H_{10}O_2$; a sesquiterpene, cadinene, $C_{15}H_{24}$; and a lactone of the composition $C_{10}H_{16}O_2$.

The most important constituent is menthol. The Pharmacopœia requires that oil of peppermint shall contain not less than 8 per cent. of esters, calculated as menthyl acetate, and not less than 50 per cent. of total menthol (free and combined), both of which may be determined according to the general directions given for the estimation of alcohols and esters on pages 682 and 683. As 1 molecule or 196.68 parts of menthyl acetate requires 1 molecule of potassium hydroxide, as shown by the equation $C_{10}H_{19}C_2H_3O_2 + KOH = C_{10}H_{19}OH + KC_2H_3O_2$, for complete saponification, each Cc. of $\frac{N}{2}$ alcoholic KOH solution, containing 0.02787 Gm. of KOH, corresponds to 0.09834 Gm. of menthyl acetate; hence in the official test the number of Cc. required must be multiplied by 9.834 (0.09834×100) and the product divided by the weight of oil taken, to obtain the percentage of esters present.

In the official test, after determination of the ester-content, the residual oil now containing all the menthol originally present in the oil of peppermint both in the free and combined state (since the latter was saponified by the treatment with alkali), is treated with acetic anhydride and in the acetylized oil thus obtained the determination of total menthol is made, after thorough dehydration with calcium chloride. From the equation given above to show the saponification of the ester, it follows that 1000 Cc. of the $\frac{N}{2}$ KOH solution represent 21 (actually 20.85) Gm. of acetyl radical in combination with the menthol; this weight is found by subtracting from the molecular weight of acetyl, 42.70, the atomic weight of hydrogen replaced in menthol by the radical during acetylization and restored by saponification of the ester, and then dividing the remainder by 2, as only $\frac{N}{2}$ alkali solution is used, thus: $42.70-1=41.70$ and $41.70 \div 2=20.85$. Hence the weight of non-acetylized oil (*i. e.*, the original oil) on which the percentage of menthol is to be based is the difference between the weight of acetylized oil taken for the determination and the weight of the acetyl radical equivalent to the number of Cc. of $\frac{N}{2}$ alkali solution required for saponification, namely 0.021 Gm. multiplied by the number of Cc. of $\frac{N}{2}$ alkali solution used. Having thus ascertained the weight of the original oil equivalent to the weight taken of acetylized oil, the percentage of total menthol can easily be found by multiplying the number of Cc. of $\frac{N}{2}$ alcoholic KOH solution required by 7.749 (0.07749, the quantity of menthol represented by 1 Cc., × 100) and dividing the resulting product by the weight of original oil.

Japanese oil of peppermint, although rich in menthol (sometimes containing 79 per cent.), is not used medicinally, on account of its peculiar bitter and disagreeable taste.

Oil of peppermint differs from other oils in the variety of its color-reaction with acids, as mentioned in the Pharmacopœia.

Oil of Pimenta or **Oil of Allspice** closely resembles oil of cloves in its constitution, but has a lower specific gravity. It contains eugenol, $C_6H_3C_3H_5.OCH_3OH$, and a sesquiterpene, $C_{15}H_{24}$; but little or nothing is known regarding other constituents that give to the oil its peculiar odor. The official requirement is for not less than 65 per cent. of eugenol, which is to be determined exactly as directed for the assay of oil of cloves.

Oil of Rose.—This oil shows a marked difference in constitution from other volatile oils, in that the solid crystallizable portion consists solely of a mixture of odorless hydrocarbons, one of which has the composition $C_{20}H_{42}$. The liquid portion of the oil, upon which its fragrance depends, is a mixture of geraniol, linalool, citronellal, citral and phenylethyl alcohol. It has been found adulterated with the oils of geranium and palmarosa, guaiac-wood oil and spermaceti; the latter may be detected by the congealing-point and saponification value. The congealing-point should lie between 18° and 22° C. (64.4°–71.6° F.) and in the case of oil of rose is that point at which the first crystals separate when the oil is slowly cooled. The Pharmacopœia also requires determination of the saponification value of oil of rose, which should be not less than 10 nor more than 17—that is, 1 Gm. of oil should require not less than 0.010, nor more than 0.017, Gm. of potassium hydroxide when tested as officially directed.

Oil of Rosemary.—The constituents of this oil are pinene, cineol, borneol, camphor and bornyl acetate, $C_{10}H_{17}C_2H_3O_2$. Several commercial varieties of the oil are known, as English, French, Italian and Spanish, the Eperlé brand being considered the finest in this country. Oil of rosemary is dextrogyrate; it is soluble in ½ its volume or more of 90 per cent. alcohol, also in 10 volumes of 80 per cent. alcohol.

The Pharmacopœia requires that oil of rosemary shall contain not less than 5 per cent. of esters calculated as bornyl acetate and not less than 15 per cent. of total borneol, both determinations are made as directed for the determination of menthyl acetate and total menthol in oil of peppermint, except that different multiplication factors must be used, because the molecular weights of borneol and bornyl acetate are not identical with those of menthol and menthyl acetate, being 152.98 and 194.68 respectively. Each Cc. of $\frac{N}{2}$ alcoholic KOH solution corresponds therefore to 0.07149 Gm. of borneol or 0.09734 Gm. of bornyl acetate.

Oil of Santal.—The official or East Indian oil of sandalwood is said to consist chiefly of alcohols, to which the name santalol and the formula $C_{15}H_{25}OH$ have been applied. The oil is said also to contain an aldehyde, called santalal, $C_{15}H_{24}O$, and a sesquiterpene. It is lævogyrate, its angle of rotation should be not less than —16° nor more than —20° in a 100 Mm. tube at 25° C. (77° F.), while inferior oils produced in Australia and the West Indies are all dextrorotatory.

Oil of santal may be adulterated with cedarwood oil, gurjun balsam oil, oil of copaiba and fatty oils, which can be detected by decreased solubility in 70 per cent. alcohol, the pure oil being soluble in 5 volumes of that liquid.

The Pharmacopœia requires the presence of not less than 90 per cent. of alcohols, calculated as santalol, and the determination may be made according to the general method given on page 682; as in the case of the oils of peppermint and rosemary, the weight of acetylized oil used must be reduced to the basis of non-acetylized oil (see under Oil of Peppermint, page 696). The molecular weight of santalol being 220.53, each Cc. of $\frac{N}{2}$ alcoholic KOH solution used corresponds to 0.11026 Gm. of santalol and to 0.13116 Gm. of santalyl acetate, and to ascertain the percentage of santalol present, the number of Cc. of the alkali solution required must be multiplied by 11.026 (0.11026×100) and divided by the weight of acetylized oil taken less the number of Cc. of the KOH solution multiplied by 0.021.

Oil of Sassafras.—The chief constituent of oil of sassafras is safrol, $C_{10}H_{10}O_2$, about 80 per cent., with a very small amount of eugenol, about 10 per cent. of terpenes, pinene, and phellandrene, and about 7 per cent. of camphor.

Safrol, at ordinary temperatures, is a colorless liquid of 1.108 specific gravity at 15° C. (59° F.); it is also found in Japanese camphor oil, from which it is now largely obtained. Sassafras oil is frequently adulterated with camphor oil. A perfectly pure article appears to be of rare occurrence. Inasmuch as camphor oil contains all of the constituents found in sassafras oil, the detection of the former is exceedingly difficult, but its presence may be indicated by strong variations in the specific gravity and other physical properties. Under the name of artificial sassafras oil, fractions of camphor oil having a specific gravity similar to that of true sassafras oil are sold.

Oil of Savin.—This oil was formerly supposed to consist only of hydrocarbons, but is now known to be chiefly composed of an alcohol, sabinol, $C_{10}H_{15}OH$, 10 per cent. and its ester, sabinol acetate, $C_{10}H_{15}C_2H_3O_2$, 40–44 per cent., together with cadinene, and possibly cuminic aldehyde. The commercial oil is largely adulterated, comparatively little of the pure oil being offered for sale; not more than 25 per cent. should distil below 200° C. (392° F.).

Oil of Spearmint.—In composition oil of spearmint differs radically from oil of peppermint, containing lævorotatory limonene and lævorotatory carvone, $C_{10}H_{14}O$, with possibly some lævorotatory pinene.

Oil of Tar.—This oil, formed during the dry distillation of wood, is obtained from pine tar by fractional distillation. It is a complex mixture of hydrocarbons, acetic and other acids, and undetermined empyreumatic products.

Oil of Thyme.—The most important constituent of this oil is thymol, $C_{10}H_{14}O$, or $C_6H_3CH_3C_3H_7OH$, a monatomic phenol; the hydrocarbon cymene, $C_{10}H_{14}$, is also present, as well as very small quantities of pinene. The phenol-content of the oil varies, as a rule, between 20 and 25 per cent., occasionally, but rarely, rising to 40 per cent. French, likewise German, oil of thyme contains chiefly thymol, although sometimes its isomer carvacrol is also present. The Spanish oil contains carvacrol and the phenol-content rises as high as 50–70 per cent. at times. Oil of thyme is frequently adulterated with oil of turpentine.

The Pharmacopœia requires the presence of not less than 10 per cent. of phenols, which may be determined as directed under Oil of Cloves; more accurate results will, however, be obtained by the iodine method given on page 684.

In order to determine whether the oil contains thymol or carvacrol, the alkaline solution of phenylate is separated from the oil, transferred to a separating funnel, and acidulated with sulphuric acid. After the phenol has completely separated, the aqueous solution is run off and the oil set aside in a capsule in a cool place. If the oil consists of thymol, it solidifies upon standing, or crystallization may be induced by adding a fragment of a thymol crystal. If it consists of carvacrol the oil remains liquid. If both phenols are present it crystallizes partially.

Oil of Turpentine.—The official oil, derived from American turpentine, consists almost wholly of dextrorotatory pinene, which, in the crude oil, is associated with rosin and other oxidation-products, depending upon age and exposure. These impurities, being removable by treatment with sodium hydroxide solution and subsequent distillation, are therefore not present in the official *rectified* oil, which alone should be employed for internal use.

Allied and Derivative Products.—The Pharmacopœia recognizes several compounds which, being allied to or directly obtained from volatile oils, should be considered at this point.

Benzaldehyde, C_7H_6O or C_6H_5COH.—This, the chief constituent of the volatile oil of bitter almond, and known also as artificial or synthetic oil of bitter almond, is now separately recognized. It differs from the natural oil of bitter almond mainly in the absence of all hydrocyanic acid.

It may be obtained from the volatile oil of bitter almond, peach, apricot, and other seeds by shaking the oil with 2 or 3 times its weight of a concentrated solution of acid sodium sulphite, whereby crystalline sodium benzalhydroxysulphonate is formed. The latter compound is washed with cold alcohol and treated with a strong solution of sodium carbonate, which causes the regeneration of benzaldehyde, and this is then rectified by distillation with steam. Synthetically, benzaldehyde is prepared either from benzyl chloride, $C_6H_5CH_2Cl$, or benzylene dichloride, $C_6H_5CHCl_2$, both of which may be obtained by treatment of boiling toluene with chlorine gas. In the case of benzyl chloride, this compound is heated with either lead or barium nitrate, while a stream of carbon dioxide is passed through the mixture; the resulting benzyl nitrate decomposes with the formation of benzaldehyde and oxides of nitrogen. In the case of benzylene dichloride, this may be heated with water to 150° or 160° C. (302° or 320° F.), when benzaldehyde and hydrochloric acid are formed. In both cases the benzaldehyde produced is further purified by treatment with acid sodium sulphite, as stated above.

Like oil of bitter almond benzaldehyde is soluble in 300 parts of water, and when exposed to air readily oxidizes to benzoic acid. It is, however, not poisonous like the natural oil.

The Pharmacopœia requires that official benzaldehyde shall contain not less than 85 per cent. of true C_6H_5COH, which is directed to be determined as follows: Carefully weigh 10 Cc. of purified kerosene into a tared 150 Cc. flask, add 12 drops of benzaldehyde, and note the weight of the latter; add 20 Cc. of distilled water with 6 drops of phenolphthalein test-solution and neutralize the liquid exactly with sodium hydroxide solution. Now add from a burette gradually a 20 per cent. sodium sulphite solution, alternating with $\frac{N}{2}$ hydrochloric acid from a second burette, until 10 Cc. of the sulphite solution have been added, and enough acid to maintain a neutral reaction; after adding a little more phenolphthalein solution and agitating the flask frequently, set it aside for two hours and then note the quantity of $\frac{N}{2}$ acid used. At the same time carry out a blank test, identical with the foregoing, except that the benzaldehyde is omitted, and note the quantity of $\frac{N}{2}$ acid used. Now subtract the number of Cc. of acid required in the blank test from the number required in the first operation, which will indicate the number of Cc. required for the benzaldehyde; multiply this difference by 5.26 (or 0.0526 and then by 100) and divide the product by the weight of benzaldehyde used for the test, to ascertain the percentage of true C_6H_5COH present in the sample. As already stated under oil of lemon, sodium sulphite shows an alkaline reaction toward phenolphthalein, and acid sodium sulphite shows a neutral reaction. Hence, in the above test, when the latter salt is formed by addition of hydrochloric acid, the reaction remains neutral until a corresponding quantity of sodium benzalhydroxysulphonate has been formed, and finally, when all benzaldehyde has been taken up, permanent neutrality appears with an excess of acid sodium sulphite. Since each molecule, or 105.26 parts, of absolute aldehyde requires 1 molecule of acid sodium sulphite, to form which 1 molecule of absolute hydrochloric acid is required to react with 1 molecule of sodium sulphite, each Cc. of the $\frac{N}{2}$ acid required by the benzaldehyde and containing 0.01809 Gm. of HCl, corresponds to 0.0526 Gm. of C_6H_5COH, for 36.18 : 105.26 :: 0.01809 : 0.0526.

Camphor.—This term is applied to compounds having the composition $C_{10}H_{16}O$, which occur in a number of essential oils and are solid at ordinary temperature. They are no doubt the result of oxidation of hydrocarbons in the plant, and stand in the relation of a ketone to the alcohol borneol, $C_{10}H_{17}OH$. Official camphor is derived solely from the wood of the camphor tree of China and Japan. When camphor wood is heated in stills the camphor volatilizes and sublimes in the form of small grains, which come to this country as crude camphor. It is accompanied, as a by-product, by *oil of camphor*, a liquid of complex composition, containing not less than four hydrocarbons, pinene, phellandrene, dipentene, and cadinene, besides five oxidized bodies, cineol, camphor, terpineol, safrol, and eugenol.

In 1902 a patent was obtained in this country for the synthetic manufacture of camphor, the method being based on the interaction of anhydrous oil of turpentine with anhydrous oxalic acid at a temperature of 120°–130° C. (248°–266° F.). The chief products obtained are camphor and borneol, which may be separated by treatment with lime and subsequent distillation; the borneol can be converted into camphor by oxidation. Synthetic camphor thus made resembles the natural product closely in appearance and properties, having about the same specific gravity, melting-point, and boiling-point, but showing a much lower angle of rotation. The manufacture of synthetic camphor is now carried on to a limited extent.

Cinnamic Aldehyde, C_9H_8O or $C_6H_5.CH : CH.COH$.—Both the natural aldehyde found in oil of cinnamon and that synthetically prepared are officially recognized under the Latin title Cinnaldehydum.

The natural product is obtained from oil of cassia by the same method as given for benzaldehyde from oil of bitter almond. The crystalline compound, after being washed with cold alcohol, is decomposed with dilute sulphuric acid, and the regenerated cinnamic aldehyde then rectified by distillation. Synthetically cinnamic aldehyde may be prepared by diluting a mixture of 10 parts of benzaldehyde, 15 parts of acetaldehyde, and 10 parts of 10 per cent. sodium hydroxide solution, with 900 parts of water, and setting the liquid aside for several days, when the two aldehydes will condense to form cinnamic aldehyde with elimination of water, thus: $C_6H_5COH + CH_3COH = C_6H_5CH.CH.COH + H_2O$.

The Pharmacopœia requires that official cinnamic aldehyde shall contain at least 95 per cent. of the pure aldehyde, the determination being made exactly as directed for the assay of citral in oil of lemon, except that a correspondingly smaller quantity of cinnamic aldehyde is used for the test. As in the case of oil of lemon, 2 molecules of acid sodium sulphite are concerned in the reaction with 1 molecule of the aldehyde, and hence 1 molecule of cinnamic aldehyde or 131.07 parts will require 2 molecules or 72.36 parts of absolute hydrochloric acid for formation of the necessary quantity of acid sodium sulphite, which quantity of acid corresponds to 4000 Cc. of the $\frac{N}{2}$ acid; each Cc. of the latter, containing 0.01809 Gm. of HCl, must therefore correspond to 0.033 (or more accurately 0.03277) Gm. of pure cinnamic aldehyde, for 72.36 : 131.07 : : 0.01809 : 0.03277.

Eugenol, $C_{10}H_{12}O_2$ or $C_6H_3(OH)(OCH_3).C_3H_5$.—Chemically this compound is also known as allylmethylpyrocatechol; it belongs to the class of phenols and is the chief constituent of oil of cloves, besides being present in other oils. It is obtained by shaking oil of cloves with an excess of 10 per cent. sodium hydroxide solution, whereby it is dissolved in the form of sodium eugenol. After washing the aqueous liquid with ether, it is decomposed with diluted sulphuric acid, the separated eugenol washed with sodium carbonate solution to remove adhering acid, and finally distilled.

Upon oxidation with potassium permangante eugenol yields vanillin. As it is used for the manufacture of the latter substance, it is sometimes abstracted from oil of cloves, which thus loses materially in value.

Eucalyptol, $C_{10}H_{18}O$.—This compound, also known as cineol, constitutes the most important portion of the oils of cajuput and eucalyptus; it is present also in oil of rosemary and the volatile oil of santonica, *artimisia pauciflora*, is composed almost wholly of eucalyptol. Chemically it is a neutral oxide, but forms crystalline compounds with hydrochloric acid gas and with phosphoric acid. It may be obtained from the oils containing it by subjecting these to low temperatures and then draining off the adhering liquid, but this process is not very satisfactory; more desirable methods are to convert the eucalyptol into its crystalline compounds, as hydrochloride or phosphate, by treating the oil with hydrochlóric acid gas or phosphoric acid, and then decomposing the product with warm water, when the liberated eucalyptol will rise to the surface and may then be washed with dilute alkali solution and distilled.

Menthol, $C_{10}H_{19}OH$.—This body, forming the chief constituent of oil of peppermint, is obtained now almost altogether from the Japanese oil by simple refrigeration, and is then purified by recrystallization. Its chemical character is that of a secondary alcohol, yielding by moderate oxidation with potassium dichromate and sulphuric acid a ketone, *menthone*, $C_{10}H_{18}O$, and combining with organic acids to form compound ethers, such as menthyl acetate, benzoate, butyrate, formate, etc. By means of dehydrating agents, menthol is converted into the hydrocarbons menthene and dimenthene.

Menthol is only slightly soluble in water, but imparts to it its odor and taste; it is readily soluble in alcohol, ether, and chloroform. When triturated with an equal weight of camphor, hydrated chloral, or thymol, it liquefies. The presence of thymol in menthol may be detected by the appearance of a green color upon adding 3 drops of sulphuric acid and 1 drop of nitric acid to a solution of a few grains of menthol in 1 Cc. of glacial acetic acid.

Methyl Salicylate, $CH_3C_7H_5O_3$ or $C_6H_4(OH)COOCH_3$.—This compound, also known as artificial or synthetic oil of wintergreen, is an ester which constitutes very nearly the whole of the natural oil of sweet birch and oil of wintergreen. It is prepared synthetically for commercial purposes by heating methyl alcohol and salicylic acid together in the presence of sulphuric acid. The reaction occurring may be shown by the equation $C_6H_4(OH)COOH + CH_3OH = C_6H_4(OH)COOCH_3 + H_2O$; the sulphuric acid serving merely to remove the water as fast as eliminated. The newly formed methyl salicylate floats on the surface of the acid liquid and is subsequently rectified by distillation.

For flavoring purposes, methyl salicylate may be used in place of the oils of betula and wintergreen.

Monobromated Camphor, $C_{10}H_{15}BrO$ or $C_9H_{15}BrCO$.—This compound is obtained by heating camphor and bromine together in a flask or retort (preferably with the addition of water or chloroform) until reaction ceases, then allowing the yellowish solution to crystallize, heating until the mass becomes white, and recrystallizing from alcohol or petroleum benzin. The reaction involves the formation of camphor dibromide, $C_{10}H_{16}OBr_2$, which splits up into camphor monobromide and hydrobromic acid, $C_{10}H_{16}OBr_2 = C_{10}H_{15}BrO + HBr$, the latter distilling over with the water or chloroform.

Safrol, $C_{10}H_{10}O_2$ or $C_6H_3.C_3H_5(OOCH_2)$.—Chemically this compound is the methylene ether of allyl pyrocatechol, and is found in several volatile oils, notably the oils of camphor and sassafras. Although oil of sassafras contains as much as 80 per cent. of safrol, the latter is commercially obtained chiefly from red oil of camphor by fractional distillation, the fraction boiling at about 230° C. (446° F.) being collected and purified by repeated chilling and crystallization.

At ordinary temperature safrol is a colorless or faintly yellow liquid, but if cooled to —20° C. (—4° F.) it solidifies to a crystalline mass, which does not again melt until warmed to 11° C. (51.8° F.). It is highly poisonous.

Terebene.—This preparation is obtained by the action of concentrated sulphuric acid on oil of turpentine, the acid being gradually added to the oil; the mixture is allowed to stand for a day, after which the supernatant layer is removed, neutralized with chalk, and distilled. Terebene differs materially from oil of turpentine, consisting chiefly of dipentene and terpinene, with, perhaps, some cymol and camphene, but its composition will vary to some extent with the particular kind of oil of turpentine used in its manufacture, the products from American, French, and Russian oils not being identical. It is optically inactive, and in this respect differs from oil of turpentine, but it must not be overlooked that a fraudulent article may have been produced by careful mixture of dextrorotatory and lævorotatory oils of turpentine, resulting in an optically inactive liquid. The specific gravity of terebene is about 0.85 at 25° C. (77° F.), and the Pharmacopœia gives the boiling-point as between 155° and 165° C. (311° and 329° F.), whereas Power and Kleber (1894) claim that true terebene carefully prepared boils between 170° and 185° C. (338° and 365° F.). Like oil of turpentine, terebene is soluble in 3 volumes of alcohol. It should be preserved in a cool, dark place in well-stoppered bottles.

Terpin Hydrate, $C_{10}H_{18}(OH)_2 + H_2O$.—This compound may be obtained by allowing a mixture of four parts of rectified oil of turpentine, 3 parts of 80 per cent. alcohol, and 1 part of nitric acid to stand in large, shallow dishes for several days; the crystals which have separated may then be drained, dried between filter paper, and recrystallized from 95 per cent. alcohol rendered slightly alkaline to remove adhering acid. The yield is about 12 per cent. of the weight of the oil of turpentine used, and the operation should always be performed in the cold, as, during hot weather, resinification of the oil will occur in place of the formation of crystals. Terpin hydrate, when fused or rendered anhydrous over sulphuric acid, yields terpin, $C_{10}H_{18}(OH)_2$, a diatomic alcohol, which, when distilled with moderately dilute sulphuric acid, loses water and is changed chiefly into terpineol, $C_{10}H_{17}OH$, a substance largely employed in perfumery on account of its very fragrant odor, resembling that of fresh lilacs.

Thymol, $C_{10}H_{14}O$ or $C_6H_3.CH_3.C_3H_7OH$.—This body, chemically known as methyl-propyl phenol, occurs in several volatile oils, and is obtained by treating the residue left upon distilling the oils below 200° C. (392° F.) with solution of sodium hydroxide, whereby thymol is dissolved as sodium thymol, $C_{10}H_{13}ONa$. When the solution has become clear by subsidence, thymol is liberated by means of hydrochloric acid and purified by distillation and crystallization; if necessary, it is also decolorized by treatment with animal charcoal.

The amount of thymol present in different oils varies considerably, and for commercial purposes it is, perhaps, all collected from ajowan oil, the volatile oil of the fruit of *ptychotis coptica*, which is said to contain from 45 to 55 per cent. of thymol; the oil of *monarda punctata*, commonly known as oil of horsemint, is said also to contain over 50 per cent. of thymol.

Thymol is sparingly soluble in water, requiring about 1100 parts for solution at 25° C. (77° F.), but is readily soluble in alcohol, ether, chloroform, and fixed and volatile oils. When triturated with an equal quantity of camphor, menthol or hydrated chloral, it liquefies.

Thymol Iodide, $C_{20}H_{24}O_2I_2$ cr $(C_6H_2.CH_3.C_3H_7.OI)_2$.—Chemically, this compound is better known as dithymol diiodide, while commercially the names aristol and annidalin have been applied to it. It is obtained by adding an aqueous solution of iodine and potassium iodide to an alkaline aqueous solution of thymol, when condensation of 2 molecules of thymol occurs and 2 atoms of iodine are taken up in the phenolic groups simultaneously. The resulting bulky precipitate is washed with water and dried at a moderate temperature.

Although the Pharmacopœia has adopted the name thymol iodide for the compound, the name aristol, by which it was first introduced into medicine, will no doubt prevail. It is insoluble in water and glycerin and only slightly soluble in alcohol, but dissolves readily in ether, chloroform, and fixed and volatile oils. Thymol iodide contains about 45 per cent. of iodine, and is used both dry and in the form of ointments; in the latter case it is preferably rubbed up with a little oil of sweet almond before adding the solid fatty vehicle.

The Pharmacopœia demands the absence of iodides and alkalies, and allows not more than 3 per cent. of ash.

Vanillin, $C_8H_8O_3$ or $C_6H_3.OH.OCH_3.COH$.—This compound, chemically also known as methylprotocatechuic aldehyde, occurs naturally in vanilla bean, of which it is the odorous and active principle, to the extent of about 2 per cent. For commercial purposes it is made synthetically either from coniferin, a glucoside found in the cambium sap of pine trees, or from eugenol, the chief constituent of oil of cloves. The latter source is preferred for economical reasons.

If made from eugenol, the latter is first converted into acetylisoeugenol, $C_{10}H_{11}(C_2H_3O)O_3$, by boiling with acetic anhydride, which is then oxidized with potassium dichromate or permanganate, yielding acetyl-vanillin. Upon treatment of the latter with potassium hydroxide solution, and concentration of the liquid, it is converted into vanillin. The mixture is filtered and the filtrate, after acidulation with sulphuric acid, shaken with ether, whereby the vanillin is removed and then purified by treating the ethereal solution with an aqueous solution of acid sodium sulphite for the removal of impurities, such as vanillic acid and vanilloylcarbonic acid. The purified ethereal solution upon evaporation at a low temperature yields vanillin.

If coniferin is to be used for the manufacture of vanillin, a concentrated solution of the same is slowly added to a moderately warm solution of potassium dichromate in water and sulphuric acid, the mixture being finally heated to boiling for three hours. The process involves the hydrolysis of the glucoside, yielding coniferyl alcohol and dextrose, the former being oxidized to vanillin with elimination of aldehyde, thus: $C_{16}H_{22}O_8 + H_2O = C_{10}H_{12}O_3 + C_6H_{12}O_6$; $C_{10}H_{12}O_3 + O = C_8H_8O_3 + C_2H_4O$. The vanillin may be recovered direct by passing steam through the mixture, or it may be extracted with successive portions of ether, after filtration of the liquid, and the ether recovered, leaving the vanillin in the form of a yellowish oily liquid, which congeals to a crystalline mass after a few days, and may be purified by solution in warm water and treatment with animal charcoal, and final recrystallization.

Vanillin is soluble in 100 parts of water at 25° C. (77° F.) and readily soluble in alcohol, ether, chloroform, and glycerin. It partakes of both aldehydic and phenolic characters and unites with bases to form saline compounds, which are decomposed upon addition of an acid with precipitation of the vanillin.

Vanillin has at times been extensively adulterated, and even recently accounts have been published of gross sophistication. Benzoic acid, especially prepared for that purpose, acetanilide, boric acid, terpin hydrate, and cumarin, the odorous principle of tonka bean, have been employed, and adulteration to the extent of 50 per cent. has been frequent, and at times even as high as 90 per cent. Acetylisoeugenol has also been met with in commercial vanillin. The latter may be detected by the abnormal crystals revealed under the microscope and the beautiful red color developed with sulphuric acid, instead of the characteristic lemon-yellow color found in the case of pure vanillin.

Since vanillin is largely used for the manufacture of vanilla extracts, the addition of cumarin has often been made for the purpose of cheapening the product, and may be detected by the method suggested by Prescott and Hess, as follows: 25 to 100 Gm. of the suspected extract are heated to about 80° C. (176° F.) in an evaporating dish, adding water from time to time to keep the volume constant. After removal of the alcohol, add normal lead acetate solution, drop by drop, until no further precipitation occurs, filter through asbestos, and wash the precipitate with a few Cc. of hot water. The cooled filtrate is then extracted with repeated portions of ether or chloroform and the combined ether-extracts shaken out with successive portions of dilute ammonia (strong ammonia 1 part and water 2 parts) until the last portion used is not colored yellow. The ammoniacal solution extracts the vanillin, the latter as an aldehyde entering into combination with the ammonia, forming aldehyde-ammonia, which is very soluble in water. The ether solution is then washed with 2 Cc. of water and evaporated spontaneously or in a desiccator. The residue is exhausted with ligroin—fraction of petroleum boiling between 30° and 40° C. (86° and 104° F.)—and the residue obtained on evaporation of the same, dried at a temperature not exceeding 45° C. (113° F.), and weighed as cumarin. Cumarin may by this method also be detected in commercial vanillin, as it will not be extracted from an ether solution of the suspected article by ammonia water.

Vanillin has been used in connection with phloroglucin as a test for free hydrochloric acid in gastric juice. The reaction, better known as *Günsburg's test*, is very sensative and capable of detecting as little as $\frac{1}{20}$ per cent. of the acid. Two solutions are used, the one consisting of phloroglucin (2 Gm.) and alcohol (15 Gm.), and the other of vanillin (1 Gm.) and alcohol (15 Gm.). The test is made by mixing 3 drops of each of the solutions with 5 drops of gastric juice in a porcelain dish and warming while rotating the dish gently. In the presence of free hydrochloric acid an intensely red mirror is produced.

RESINS.

Comparatively little was known until recently regarding the chemical composition of resins which occur in plants either alone or in combination with volatile oils as oleoresins or with gums as gum resins. Investigations have been in progress for some years in the hands of Prof. Tschirch, of Berne, Switzerland, and his colaborers, and much light has already been shed upon this rather obscure subject. This much has already been established, that resins are largely composed of organic acid esters or compound ethers of certain alcohols, to which latter the general name *resinol* has been applied; some of these alcohols give reactions similar to those characteristic of the tannins, and have therefore been designated as *resinotannols*. Thus we have benzoresinol, storesinol, peruresinotannol, toluresinotannol, etc. Some resins have decidedly acid properties, while others are known to be anhydrides, as in the case of common pine resin or colophony, which is chiefly composed of abietic anhydride, $C_{44}H_{62}O_4$; one of the resins found in copaiba is a crystalline acid, called copaivic acid, having the elementary composition, $C_{20}H_{30}O_2$; the resin obtained from guaiacum wood and officially recognized as *guaiac*, consists largely (70 per cent. and over) of guaiaconic acid, $C_{19}H_{20}O_5$, to which the well-known color reactions of guaiac with oxidizing agents are due.

Resin of Scammony consists almost wholly of scammonin, $C_{34}H_{56}O_{16}$, the anhydride of scammonic acid, which behaves like a glucoside. *Jalap resin* consists of two distinct resins which can be separated from each other by ether, the one insoluble in that menstruum, and constituting about 90 per cent. of the official resin, consists almost entirely of convolvulin, $C_{31}H_{50}O_{16}$, an anhydride possessing glucosidal properties and being colorless when pure. The official *resin of podophyllum* is a complex mixture, containing an acid called podophyllinic acid, insoluble in ether, and a substance to which the name podophyllotoxin has been given; the latter, which constitutes about 50 per cent. of the official product, is said to be the active purgative principle. Both these substances are soluble in chloroform, and may be separated by addition of ether to the chloroformic solution, which precipitates podophyllinic acid; upon evaporation of the ethereal solution podophyllotoxin is obtained.

CHAPTER LIX.

ORGANIC ACIDS.

Of the large number of compounds termed organic acids, only the few that are of special interest in pharmacy have been officially recognized. Organic acids are considered as derived from hydrocarbons or their alcohols, by replacement of hydrogen or hydroxyl by the univalent group carboxyl, COOH, and vary in their basicity as one, two, or three carboxyl groups may have been taken up, carrying with them one, two, or three atoms of replaceable hydrogen, as in the case of inorganic acids. The official organic acids are acetic acid, benzoic acid, camphoric acid, citric acid, gallic acid, lactic acid, oleic acid, salicylic acid, stearic acid, tannic acid, tartaric acid, and trichloracetic acid. Diluted hydrocyanic acid, although usually reckoned among the inorganic acids, is preferably considered at this point, since cyanogen is a carbon compound probably derived from hydrocarbons by substitution of nitrogen for hydrogen. Oxalic and valeric acids, although not officially recognized, are both of interest to pharmacists, as is also meconic acid.

Acetic Acid, $HC_2H_3O_2$ or CH_3COOH.—This acid has already been considered in connection with the derivatives of cellulose on page 616.

Benzoic Acid, $HC_7H_5O_2$ or C_6H_5COOH.—Several methods are in use for obtaining this acid from benzoin, the balsamic resin from which it takes its name.

Both a dry and a wet process are employed for extracting the acid from the resin, in which it exists in a free state. The former is by sublimation, benzoin in coarse powder, which has been dried over lime, being heated in shallow iron pans covered with a porous diaphragm and connected with a suitable condenser, carefully regulated sand-bath heat being used so as to avoid contamination of the acid with other products, partly the results of decomposition, which volatilize at a temperature approaching 200° C. (392° F.). The yield of acid by this method ranges from 6 to 8 per cent. of the weight of benzoin used, the fused resin retaining a considerable portion which can be recovered by the wet method; sublimed acid is never chemically pure, being always accompanied by a volatile oil to which the peculiar odor of the acid is due.

The wet method consists in treating powdered benzoin for some time with warm milk of lime, and finally boiling the mixture and filtering while hot. The filtrate is supersaturated with hydrochloric acid, the crude benzoic acid being allowed to crystallize and then purified by resolution in boiling water, with the addition of animal charcoal, filtered and again crystallized. In this process calcium benzoate, $Ca(C_7H_5O_2)_2$, is first formed and then decomposed with hydrochloric acid, whereby benzoic acid is liberated while calcium chloride remains in solution, thus, $Ca(C_7H_5O_2)_2 + 2HCl = 2HC_7H_5O_2 + CaCl_2$. Benzoic acid obtained by this method is of fine white appearance, and devoid of the peculiar aroma of sublimed acid.

Of late years synthetic benzoic acid has been extensively produced, and the Pharmacopœia recognizes both the natural and synthetic products. The latter is made from toluene, $C_6H_5CH_3$, by passing chlorine gas into it while boiling until an increase in weight is no longer observed. Toluene is thereby converted into benzo-trichloride, $C_6H_5CCl_3$, which liquid, when treated with water under pressure, is converted into benzoic and hydrochloric acids, thus, $C_6H_5CCl_3 + 2H_2O = C_6H_5COOH + 3HCl$; the benzoic acid is separated by straining, and washed with cold water until free from hydrochloric acid. It is important in this process that the chlorine gas be passed into the boiling toluene in diffused daylight, to avoid the formation of other products.

Large quantities of benzoic acid are also made from the urine of cattle and horses, which contains hippuric acid, or benzoyl glycocoll. By boiling hippuric acid with strong hydrochloric acid, the former absorbs water and is split up into benzoic acid and glycocoll or amidoacetic acid, thus: $CH_2(NH)(C_6H_5CO)COOH + H_2O = C_6H_5COOH + CH_2(NH_2)COOH$. Benzoic acid from this source is always accompanied by a fetid odor, which is removed by recrystallization and sublimation with benzoin.

Camphoric Acid, $H_2C_{10}H_{14}O_4$ or $C_8H_{14}(COOH)_2$.—When camphor is oxidized by means of nitric acid, both camphoric and camphoronic acids are obtained. The following is the method usually pursued: About 150 Gm. of camphor are added to 2000 Cc. of 50 per cent. nitric acid contained in a long-neck flask provided with a reflux condenser, and the mixture heated on a boiling water-bath until colored vapors are no longer given off. When cool the liquid is filtered through asbestos, for the purpose of collecting the camphoric acid which has separated, and the filtrate made to yield an additional quantity of crystals by concentration to about one-fifth its volume. The crystals are dissolved in water with the aid of sodium carbonate, and the resulting sodium camphorate allowed to crystallize; after solution in water the salt is decomposed by means of hydrochloric acid, when the liberated camphoric acid will crystallize, and may then be further purified by solution in hot water, treatment with animal charcoal, and recrystallization. The acid mother-liquor, from which the crude camphoric acid is first separated, contains the second oxidation product, camphoronic acid, $C_6H_{11}(COOH)_3$.

Camphoric acid is soluble in 125 parts of water at 25° C. (77° F.), about 3½ grains to the fluidounce, and in 10 parts of boiling water; also readily soluble in alcohol and ether.

Citric Acid, $H_3C_6H_5O_7 + H_2O$ or $C_3H_4OH(COOH)_3 + H_2O$.—This acid belongs to the class known as fruit acids, and, although occurring in many plants, is obtained for use solely from lemons and limes. It is manufactured both in this country and Europe, on a large scale, from the juice of immature fruit, which contains from 6 to 8 per cent. of acid. The juice is first clarified by ebullition and then neutralized by addition of chalk, the resulting calcium citrate being washed with boiling water, in which it is sparingly soluble, and finally decomposed by means of diluted sulphuric acid; the newly formed calcium sulphate is removed by straining, the solution of citric acid being concentrated and allowed to crystallize in large wooden vats lined with lead. If necessary, the crystals of citric acid are redissolved in water, the solution being subsequently filtered through animal charcoal, to remove color, and recrystallized.

As citric acid crystallizes better from solutions containing a little sulphuric acid traces of the latter are generally found in the commercial article. Small particles of metal found adhering to the crystals and deposited in solutions thereof are lead, derived from the crystallizing vats. Contamination with crystals of tartaric acid can be readily detected by placing some of the crystals in a small dish with a little solution of potassium hydroxide; the crystals of citric acid slowly dissolve, while those of tartaric acid gradually become opaque, owing to the formation of acid potassium tartrate. The official test for the presence of tartaric and oxalic acids depends upon the solubility of potassium citrate in acetic acid, in which the tartrate and oxalate are insoluble.

The Pharmacopœia demands 99.5 per cent. purity for citric acid, to be determined by titration with normal alkali solution. Citric acid being tribasic, each molecule or 208.5 parts will require 3 molecules or 167.22 parts of potassium hydroxide for neutralization, and hence each Cc. of normal KOH solution will correspond to 0.0695 Gm. of citric acid. In the official test 34.75 Cc. of a 5 per cent. solution of citric acid are used, which will contain 1.7375 Gm. of the acid, and hence each Cc. of the alkali solution required will represent 4 per cent. of citric acid, for 0.0695 is 4 per cent. of 1.7375; to indicate 99.5 per cent. will therefore require 24.875 (practically 24.9) Cc. of the alkali solution.

During the past few years citric acid has been prepared from dextrose (grape-sugar) by action of certain fungi, known as citromyces. The yield amounts to about 55 per cent. of the weight of dextrose used, and the resulting citric acid is in every respect identical with the natural acid. The manufacture of artificial or synthetic citric acid is said to be now in progress on a commercial scale.

Solutions of citric acid gradually separate fungous growths; this can, however, be prevented by addition of 5 or 10 per cent. of alcohol.

Diluted Hydrocyanic Acid.—The official preparation of this name is an aqueous solution of gaseous hydrocyanic acid, HCN, prepared by adding 6 Gm. of silver cyanide to a mixture of 15.54 Cc. of diluted hydrochloric acid and 44.10 Cc. of distilled water, agitating well, and pouring off the clear liquid when the precipitate has subsided. The equation $AgCN + HCl = HCN + AgCl$ shows that 1 molecule or 132.96 parts of silver cyanide is capable of yielding 1 molecule or 26.84 parts of hydrocyanic acid, and hence the 6 Gm. directed, if of official (99.9 per cent.) purity, will yield 1.21 Gm. of the acid, which produces a solution of fully 2 per cent. strength. This process is especially intended for the pharmacist so that he can prepare the diluted acid in small quantities, since the solution deteriorates slowly in the course of time.

Manufacturing chemists prefer to decompose a solution of potassium ferrocyanide with sulphuric acid, in a flask or retort, and conduct the resulting vapors into distilled water. In this process the following reactions occur: 1. The formation of hydroferrocyanic acid, thus, $K_4Fe(CN)_6 + 2H_2SO_4 = H_4Fe(CN)_6 + 2K_2SO_4$; 2. The decomposition of a further portion of potassium ferrocyanide by the newly formed acid in the presence of sulphuric acid, thus, $K_4Fe(CN)_6 + H_4Fe(CN)_6 + H_2SO_4 = 6HCN + K_2SO_4 + K_2Fe(Fe(CN)_6)$, hydrocyanic acid being evolved, while potassium sulphate and potassio-ferrous ferrocyanide, or Everitt's salt, remain in the flask or retort; the latter salt is white at first, but gradually changes to blue. Aqueous vapor, of course, passes over with the vapor of the acid, both of which are usually condensed in a Liebig condenser interposed between the retort and the receiver. Distillation is continued until the volume of the mixture in the retort has been reduced to about one-half, after which the distillate is assayed and sufficient distilled water added to bring the solution to the official standard of 2 per cent. strength.

The strength of diluted hydrocyanic acid is determined by titration with $\frac{N}{10}$ $AgNO_3$ solution in the presence of ammonia with potassium iodide as indicator, exactly as explained under Potassium Cyanide on page 492. Each Cc. of the silver solution required for the appearance of a permanent precipitate corresponds to 0.005368 Gm. of hydrocyanic acid, and hence, in the official test, where 2.69 Gm. of the diluted acid are used, 10 Cc. of $\frac{N}{10}$ $AgNO$ solution will be required to show 2 per cent. of absolute HCN, for 2 per cent. of $2.69 = 0.0538$ and $0.0538 \div 0.005368 = 10.02$.

Solutions of hydrocyanic acid are unstable, hence the official diluted acid is a very unsatisfactory preparation, even if carefully kept in small, tightly closed amber vials. Good sound corks are probably preferable to glass stoppers, as they fit more closely, as a rule. Various substances, such as sulphuric and hydrochloric acids, the mixture filtered and the solution of lactic acid evaporated. Complete evaporation of the water is not practicable, since the lactic acid would undergo decomposition, the elements of water being split off and insoluble lactic anhydride formed; hence the Pharmacopœia recognizes a very strong solution in place of the absolute acid. The temperature is an important factor in the fermentation of milk, as below 25° C. (77° F.) acetic acid will be formed, above 35° C. (95° F.) butyric acid; hence the largest yield of lactic acid is produced between these two degrees of heat.

Besides the official lactic acid two other varieties occur on the market, known as concentrated and dilute lactic acid respectively; but, since neither strength nor specific gravity is specified on the label, they should not be employed by pharmacists in prescriptions or otherwise.

The reaction between lactic acid, potassium permanganate, and sulphuric acid, mentioned in the Pharmacopœia, resulting in the development of an odor of aldehyde, is due to the oxidizing effect of the potassium permanganate, the lactic acid being split up into acetaldehyde, CH_3COH, and formic acid, $HCOOH$, which latter is then still further oxidized to carbon dioxide and water.

In the assay of lactic acid, the equation $HC_3H_5O_3 + KOH$ shows that 1 molecule or 89.37 parts of absolute acid requires 1 molecule or 55.74 parts of potassium hydroxide, and hence 1 Cc. of normal KOH solution corresponds to 0.08937 Gm. of absolute lactic acid. In the official test, 4.47 Gm. of acid being used, not less than 37.5 Cc. of the alkali solution will be required to show the presence of 75 per cent. of absolute acid, for 75 per cent. of $4.47 = 3.3525$ and $3.3525 \div 0.08937 = 37.51 +$. Each Cc. of the alkali solution also represents 2 per cent. of absolute acid.

Meconic Acid, $H_2C_7H_2O_7 + 3H_2O$ or $C_5HO_2(OH)(COOH)_2 + 3H_2O$.—This acid is of interest chiefly as a constituent of opium, and also on account of its peculiar reaction with ferric chloride, which can be used as a test for preparations of opium; ferric meconate possesses a blood-red color, like that of ferric acetate and sulphocyanate, but may be distinguished from the former by its indifference to dilute hydrochloric acid, and from the latter by its indifference to mercuric chloride. Reducing agents, such as stannous chloride and alkali hypochlorites, discharge the color of ferric meconate. Meconic acid may be obtained by precipitating a concentrated infusion of opium with calcium chloride, decomposing the resulting calcium meconate with warm dilute hydrochloric acid and recrystallizing from water.

Oleic Acid, $HC_{18}H_{33}O_2$ or $CH_3(CH_2)_7CH.CH(CH_2)_7COOH$.—In the chapter on fats and fixed oils this acid has been mentioned as being found in nearly all liquid fats. It is usually obtained of variable quality in a crude state in the manufacture of candles, being then known as *red oil;* for pharmaceutical purposes the crude acid can be sufficiently purified by simply cooling the same to 5° C. (41° F.) and separating the liquid portion from palmitic and other acids. Such an acid is recognized in the Pharmacopœia. A still purer acid may be obtained by saponifying expressed oil of almond with lead oxide, dissolving the lead oleate in petroleum benzin and decomposing the solution with dilute hydrochloric acid; after removal of the benzin by evaporation, the oleic acid may be washed with water. When perfectly pure, oleic acid is colorless, odorless, and tasteless, but rapidly becomes colored upon exposure to air and light.

The test for appreciable quantities of palmitic and stearic acids, mentioned in the Pharmacopœia, depends upon the formation of lead oleate, palmitate, and stearate, the former of which is soluble in ether, while the latter two are insoluble.

Oxalic Acid, $H_2C_2O_4 + 2H_2O$ or $(COOH)_2 + 2H_2O$.—Although this acid occurs in numerous plants, chiefly in the form of acid potassium oxalate, it is obtained for the market wholly by synthetic methods. If sawdust be made into a pasty mass with strong solution of potassium hydroxide, or potassium and sodium hydroxides, the mass then heated and kept at a temperature of 205° C. (401° F.) for one or two hours and dried, a gray powder of crude alkali oxalates will be obtained; by treatment with milk of lime, calcium oxalate results, which is then decomposed with sulphuric acid, and the solution of oxalic acid is concentrated and crystallized. A much larger yield is said to be obtained by heating sodium hydroxide with carbonic oxide to 100° C. (212° F.), whereby sodium formate, $NaHCO_2$, is produced, which is then further heated to 400° C. (752° F.), with exclusion of air as far as possible, and converted into sodium oxalate, from which the acid is liberated as above.

Oxalic acid is used in medicine only in the form of ferrous and cerous oxalates, but is a valuable reagent in chemical analysis.

Salicylic Acid, $HC_7H_5O_3$ or $C_6H_4(OH)COOH$.—Since the introduction of salicylic acid into medicine, nearly all thus used has been prepared synthetically from phenol (carbolic acid); small quantities are also obtained by treating oil of wintergreen with potassium hydroxide and decomposing the resulting potassium salicylate with an acid. Natural salicylic acid, obtained by the latter method, is preferred by some physicians; it commands a much higher price than the synthetic acid. In the synthetic process the first step is the manufacture of sodium carbolate, or sodium phenol, C_6H_5ONa, by saturating phenol with sodium hydroxide. This compound is then dried and treated with carbon dioxide, whereby sodium phenol carbonate is formed, thus, $C_6H_5ONa + CO_2 = NaC_6H_5CO_3$; this is heated in tightly closed vessels, or in retorts through which a stream of carbon dioxide is passing, to 130° C.

(266° F.), when it is converted into sodium salicylate, $NaC_7H_5O_3$. This is the process now generally employed, and is a modification of Kolbe's original method, in which only one-half of the phenol was utilized, the remainder distilling over at a higher temperature. The crude sodium salicylate is dissolved in water and decomposed by means of hydrochloric acid; the resulting mixture is drained, washed with cold water, and finally dissolved in boiling water from which salicylic acid crystallizes on cooling and can be purified by solution in diluted alcohol, decolorized with animal charcoal, and recrystallized.

Salicylic acid furnishes several derivative products used in medicine, one of which is recognized in the Pharmacopœia under the name:

Phenyl Salicylate, $C_6H_5C_7H_5O_3$ or $C_6H_4(OH)COOC_6H_5$.—This compound is commercially better known as salol, which was also formerly its official title. It can also be looked upon as a derivative of phenol, but as it is more closely allied to salicylic acid in its therapeutic effects, it is generally considered together with the same. Several methods are known for preparing phenyl salicylate, such as treating a mixture of sodium phenol and sodium salicylate with phosphorus oxychloride, or passing a slow current of phosgene (carbonyl chloride) into a warm mixture of the two salts; in both cases new sodium salts are formed as by-products, and the resulting phenyl ester is dissolved in alcohol and crystallized. A later and simpler process consists in heating salicylic acid, contained in a flask with a long, narrow neck, in an oil-bath, to 220° or 230° C. (428° or 446° F.); air is excluded by passing a stream of carbon dioxide into the flask, the long neck of which permits only vapors of water and carbon dioxide to escape. The salicylic acid is first changed by heating into its anhydride, thus, $2HC_7H_5O_3 = (C_6H_4(OH)CO)_2O + H_2O$; this is then split up into phenyl salicylate and carbon dioxide, thus: $(C_6H_4(OH)CO)_2O = C_6H_5C_7H_5O_3 + CO_2$. The resulting compound is dissolved in alcohol and crystallized, as in the other methods.

Among other derivatives of salicylic acid introduced into medicine may be mentioned: *aspirin*, or acetylsalicylic acid; *salipyrine*, or antipyrine salicylate; *saliphen*, compound of salicylic acid and phenetidin; *salophen*, a compound of salicylic acid and acetylamidophenol, a group far less poisonous than phenol; *cresalol* or cresyl salicylate, etc., which are more fully described in the *National Standard Dispensatory*.

Stearic Acid, $HC_{18}H_{35}O_2$ or $C_{17}H_{35}COOH$.—This acid, which is of very little use in pharmacy, except in the preparation of glycerin suppositories, is largely obtained in the manufacture of glycerin from tallow, by treatment with water and superheated steam, as explained on page 676. The commercial article is frequently impure, often consisting wholly of stearin; for pharmaceutical purposes it should, at least, respond to the official requirement regarding the limit of undecomposed fat. Solubility in alcohol also serves to distinguish stearic acid from stearin.

Tannic Acid, $HC_{14}H_9O_9$ or $C_{13}H_9O_7.COOH$.—The official tannic acid is more specifically known as gallotannic acid, from its source, nut-gall, to distinguish it from related compounds found in the bark of various oaks, chestnuts, etc.; it has, however, also been met with in the leaves of tea and sumac. Absolutely pure gallotannic acid is probably digallic acid, or an anhydride of gallic acid, as stated on page 712, but its constitution as such has not yet been clearly defined. The commercial article is, however, as a rule, contaminated with variable proportions of glucose in weak combination, which formerly gave support to the view that tannic acid was a glucoside. The true chemical character of tannin was first announced by Schiff, in 1871, and corroborated by Etti, in 1884. The subject of the various tannins has been carefully studied in this country by the late Prof. H. R. Trimble, who laid down the results of his labors in a valuable and extended monograph, entitled *The Tannins*, from which work much of the information here given has been taken.

Different methods are employed by manufacturers for the extraction of gallotannic acid, giving rise to the varieties known as ether-, alcohol-, and water-tannin. Chinese or Japanese galls are preferred to the Turkish variety, on account of their richness in tannic acid, from 60 to 65 per cent., and greater freedom from coloring matters. The ether method yields the best product. The finely cut galls are first exhausted with water, at a temperature of 40° or 60° C. (104° or 140° F.); the infusion is allowed to cool, then filtered and intimately mixed with commercial ether by agitation. When the emulsion has separated, the upper ethereal layer, containing coloring matter, resin, fat, gallic and ellagic acids, is removed and the aqueous fluid, after concentration, under reduced pressure, in a still, to a syrupy consistence, is spread, when cool, on tin plates, which are placed on a steam table and covered with a wooden box; this causes the tannin to puff up and dry and gives rise to the peculiar spongy character of commercial tannin. The so-called crystalline tannic acid of German manufacturers is obtained by introducing a very thick syrupy mass, prepared as above stated, into well-tinned copper vessels, with a perforated bottom, through which the mass slowly drops in long threads on to heated revolving cylinders, where it dries, and is removed in the form of thin, needle-shaped particles.

Another plan is to extract the powdered nutgall with a mixture of ether four parts and alcohol one part, transferring the tannic acid to water by agitation with the latter, and then proceeding as before stated. This method is extensively employed.

Diluted alcohol is used in the preparation of alcohol-tannin by percolation, the tincture being concentrated and evaporated to dryness in a vacuum apparatus. Water-tannin is obtained by evaporating the aqueous infusion described above, to dryness, in a vacuum-pan. Neither of these products is as free from color or impurities as the first named or ether-tannin.

In 1893 Prof. Trimble suggested the use of acetone for the extraction of tannic acid from nutgall, and exhibited, at Chicago, a sample of the acid, almost white, prepared by this method. The advantages claimed for this solvent are cheapness, thorough penetration, and rapidity of action.

Glucose, the most persistent impurity found in tannin, can be removed completely, as suggested by Trimble, by treatment with lead acetate and hydrogen sulphide and subsequent extraction of the tannin with acetic ether.

Gallotannic acid differs markedly from oak-bark tannins in its behavior toward several reagents, thus, while with lime water oak-tannins give a pink or red precipitate, gallotannic acid causes a blue precipitate; with bromine water gallotannic acid gives no precipitate, while oak-tannins cause a yellow precipitate; ferric chloride and ammonium hydroxide cause a green precipitate with oak-tannins and a blue one with gallotannic acid, etc. The blue color sometimes observed in the case of oak-tannins with ferric salts is due to the presence of a foreign substance, pure oak-tannins showing only a green color. (Trimble.)

Owing to the ready discoloration of tannic acid by metallic iron in the presence of moisture, all contact with spatulas under such conditions must be avoided. Solutions of tannic acid change readily, particularly if exposed to air and light, gallic acid and probably *ellagic acid*, $C_{14}H_8O_9$, being gradually formed; such changes are retarded and even prevented by the presence of glycerin or alcohol in sufficient quantity.

The term tannin is now applied to the whole group of vegetable astringents, while the name tannic acid has been reserved for the particular product derived from nutgalls. The classification adopted by Trimble divides all tannins into two main groups, which may be distinguished from each other by the reactions above mentioned. All tannins should be soluble in water and precipitated by gelatin. The gallotannic-acid group includes, besides nutgall tannin, the tannins found in chestnut wood, chestnut bark, pomegranate bark, and sumac, while the oak-tannin group comprises the tannins from different species of oak, from kino, gambir, krameria, tormentil, mangrove, and canaigre.

While, for technical purposes, the estimation of tannin in various tanning materials is often of importance, and is no doubt also valuable in chemical plant analysis, such determinations are not required in pharmacy. Advantage is taken of the well-known property of tannin to form insoluble compounds with gelatin (as demonstrated in the preparation of leather), and this operation is included in all methods of assay thus far published. A complete account of Löwenthal's method for estimating tannin, as modified by Von Schroeder, will be found in the *National Standard Dispensatory*, p. 89.

Tartaric Acid, $H_2C_4H_4O_6$ or $(CHOH)_2(COOH)_2$.—This acid is even more widely distributed in the fruit of many plants than citric acid, occurring both in the free and combined state. For commercial purposes, it is obtained from crude or partially purified argols (see p. 488) by neutralizing the acid potassium tartrate in hot solution with chalk, whereby calcium and potassium tartrates are formed, and then decomposing the remaining potassium tartrate with calcium chloride; the resulting calcium tartrate is washed with water until tasteless and decomposed by digestion with sulphuric acid, when sparingly soluble calcium sulphate is formed and tartaric acid liberated, which latter enters into solution. After removal of the precipitated calcium sulphate by filtration, the solution of tartaric acid is concentrated and allowed to crystallize, the crystals, if necessary, being redissolved, digested with animal charcoal, and recrystallized.

Tartaric acid is rarely found in the shops in other than powder form, and, as a rule, is free from impurities. The official test for oxalic acid, by means of calcium sulphate solution, depends upon the insolubility of calcium oxalate in the presence of ammonium salts, whereas calcium tartrate is but slowly deposited under like conditions; an excess of ammonia must be avoided, hence the Pharmacopœia directs incomplete neutralization. If crystallized tartaric acid is contaminated with uvic acid, the latter is readily detected by the milk-white appearance of its crystals, those of tartaric acid being translucent.

Trichloracetic Acid, $HC_2Cl_3O_2$ or CCl_3COOH.—This acid has already been considered in connection with Acetic Acid on page 613.

Valeric Acid, also known as Valerianic Acid, $HC_5H_9O_2$ or $(CH_3)_2CH.CH_2.COOH$.—As this acid occurs in a free state in valerian root, it may be obtained by distilling the root with water, neutralizing the aqueous portion of the distillate with sodium hydroxide, and decomposing this solution with sulphuric acid; it may then be purified by fractional distillation.

Commercially the acid is made by oxidation of amyl alcohol with a mixture of potassium dichromate and sulphuric acid, and neutralizing the distillate with sodium hydroxide; the resulting sodium valerate is decomposed by means of sulphuric acid, when the liberated valeric acid will rise as an oily layer. This is then freed from water by treatment with sulphuric acid, and carefully distilled. The reaction taking place may be illustrated thus: $3C_5H_{11}OH + 2K_2Cr_2O_7 + 8H_2SO_4 = 3HC_5H_9O_2 + 2K_2SO_4 + 2Cr_2(SO_4)_3 + 11H_2O$. Since a small portion of the amyl alcohol escapes oxidation, it is attacked by the newly formed acid and passes over into the distillate as a compound ether, known as *amyl valerate*, $C_5H_{11}C_5H_9O_2$; the name *apple oil* is given to this ester on account of its apple-like odor when diluted. When the acid distillate is neutralized with sodium hydroxide the amyl valerate separates as an oily liquid, and may be removed.

The solubility of valeric acid in not less than 26, and not requiring over 30 times its weight of water, affords a ready means of discovering certain impurities; it should also produce a clear solution with a slight excess of ammonia water.

The only use made of valeric acid in pharmacy is for the production of ammonium valerate in the manufacture of the elixir of the same name.

CHAPTER LX.

ALKALOIDS.

THE name alkaloids is applied to a large class of carbon compounds containing nitrogen, which are capable of neutralizing acids and forming salts. The basic properties of these compounds vary in intensity, some exhibiting but a feeble basic reaction, while others are capable of decomposing heavy metallic salts with the formation of metallic hydroxides. The term alkaloid was given to these so-called organic bases on account of their similarity in chemical character to alkalies, alkaloid meaning alkali-like.

Since the discovery of basic principles in both living and dead animal tissues the name alkaloids has generally been restricted to those nitrogenous bases derived from plants, the term *leucomaines* having been selected for the basic substances found in living animal tissues and *ptomaines* for those produced during putrefaction of dead animal tissues; the last named are still sometimes called cadaveric alkaloids. Chemists go even a step further by subdividing vegetable bases and reserving the name alkaloid for all those shown to be derived from pyridine, C_5H_5N, or quinoline, C_9H_7N, two simple bases found in coal tar.

The discovery of alkaloids occurred early in the last century, when Sertürner, a German apothecary, in 1817, demonstrated the basic character of a substance obtained by him, in 1806, from opium, now known to us as morphine. Since then the number of alkaloids determined has increased rapidly, although their occurrence is confined to comparatively few plant families, for instance, the apocynaceæ, leguminosæ, liliaceæ, loganiaceæ, papaveraceæ, ranunculaceæ, rubiaceæ, rutaceæ, solanaceæ, umbelliferæ, and perhaps one or two others. Sometimes the same alkaloid is found in more than one family, as in the case of the alkaloid berberine, but the occurrences are rare. As a rule, alkaloids are not restricted to special parts of plants; while present to a much larger extent in the root, bark, fruit, and seed of different plants, in a few cases the leaves are the chief source, and in some cases the same alkaloids are found in every part of the plant. In order to distinguish the basic from neutral vegetable principles a different terminology has been adopted for the two classes, which has been maintained in the Pharmacopœia, and serves an excellent purpose. The ending *ine* (Latin *ina*) is applied to all basic plant products, while the ending *in* (Latin *inum*) is given to all neutral principles.

While all alkaloids contain nitrogen, a few do not contain oxygen.

The latter are, as a rule, colorless liquids when freshly obtained and not exposed to the air, and can be distilled without decomposition; they are generally characterized by a peculiar strong odor, as in the case of coniine, nicotine, and sparteine. Alkaloids containing oxygen are generally without odor and, as a rule, crystallizable, a few also occurring in the liquid state. With the exception of codeine, colchicine, pelletierine, and physostigmine, alkaloids are difficultly soluble in water, but all dissolve readily in alcohol, and some, but not all, dissolve in amyl alcohol, benzene, chloroform, ether, and ethyl acetate. Vegetable bases do not all possess the same saturating power, for while the majority are monacid in their character, several well-defined diacid bases are known. When brought together with acids they do not, like inorganic bases, cause the displacement of basylous hydrogen with the formation of water, but form salts by simple addition. Inasmuch as alkaloids are closely related to ammonia and often designated as substituted ammonias, it has been suggested that the same view be taken in regard to the formation of their salts with acids, as in the case of ammonia, namely, that when in solution in water they take up the elements of water and then unite with the acids with elimination of water, as, for instance, $NH_3 + H_2O = NH_4OH$ and $NH_4OH + HCl = NH_4Cl + H_2O$; $C_{17}H_{19}NO_3$ (morphine) $+ H_2O = C_{17}H_{20}O_3NOH$ and $C_{17}H_{20}O_3NOH + HCl = C_{17}H_{20}O_3NCl + H_2O$. This view is not expressed in the formulas and the nomenclature of the Pharmacopœia, but may in the course of time become more generally accepted. In regard to the naming of salts formed by the union of alkaloids with acids, it is customary in the case of oxygen acids to follow the usual rule, thus: acetates, citrates, nitrates, phosphates, sulphates, etc., but in the case of halogen acids, the proper name would seem to be obtained by changing the termination *ic* of the acid into *ide* for the salt, thus hydrobromide, hydrochloride, hydrocyanide, etc.

In nature alkaloids rarely occur in a free state, being usually associated with an acid, which, in some instances, is a peculiar acid characteristic of the plant in which it is found, as quinic acid of the cinchona barks, meconic acid in opium, etc.; many alkaloids occur in the plant as tannates. Occasionally the alkaloid exists partly in combination and partly in the free state, as in the case of hydrastine. For their extraction various methods are employed; either the finely comminuted drug is exhausted with acidulated water, whereby the alkaloid is brought into solution as a new salt, which can then be decomposed and precipitated by means of an alkali and further purified by resolution in some appropriate solvent, filtration through animal charcoal, and crystallization; or the drug may be exhausted with a neutral solvent, such as alcohol or diluted alcohol, the resulting tincture being acidulated, evaporated to remove fats, resins, etc., filtered, treated with water, and precipitated and purified as stated above. Advantage is taken of the difference in solubility between free alkaloids and their salts to separate and purify the product by the use of immiscible solvents, such as water and petroleum benzin, water and chloroform, water and ether, etc., whereby the alkaloid can be alternately transferred, in a combined or free state, from one fluid to another; this necessitates, of course, provision for bringing the liquids into intimate contact by agitators. This method, which is extensively employed in the assay of alkaloidal drugs, is termed by analysts the "shaking out process," because, on a small scale, the transfer is made in glass separators by rotation or shaking. In large operations, such as the manufacture of the cinchona alkaloids and others, kerosene or gasolin, closely allied to benzin, is now extensively employed on account of its solvent capacity, its cheapness, and ready separation from watery fluids. In the case of alkaloids which are volatile, the drug is placed in a still with some water, and, by the addition of a fixed alkali, the alkaloid is liberated, and, with the aid of heat, passed over into a receiver containing acidulated water, when, having been obtained as an acid salt, it can be further purified and isolated by one of the methods before mentioned.

To determine the presence of an alkaloid in any drug, the simplest plan is to macerate a small portion of the finely powdered article with about ten times its weight of Prollius' fluid, a liquid of remarkable penetrating power, composed of ether 325 Cc., alcohol 25 Cc., and stronger water of ammonia 10 Cc. The maceration should be conducted in a well-closed flask, for several hours, with frequent agitation, after which some of the clear liquid is decanted into a glass separator (see page 158) containing some 5 per cent. sulphuric acid, and, by means of careful but active rotation, any alkaloid present is transferred to the acid fluid; upon withdrawing this and warming on a water-bath to remove ether and alcohol, the addition of any of the general reagents mentioned below will produce a cloudiness or precipitate if alkaloids have been extracted.

Although particular alkaloids are only found in certain plants or species of plants, it often happens that several alkaloids are present in the same plant, ranging from 2 in nux vomica to 21 in opium and 32 in cinchona; rarely, however, does the number exceed 4. When pure, alkaloids are, as a rule, crystallizable, excepting the amines or liquid bases, without color, and have a definite melting-point, which latter is an important test of purity; their different solubilities have already been referred to. In solution, whether free or in a combined state, they are precipitated by a number of substances which are known as alkaloidal class reagents, and therefore incompatible with them in prescriptions. Such reagents are tannic acid, picric acid, and mercuric chloride; besides these, the following tests for the presence of alkaloids are known by special names—*Mayer's reagent*, a solution of potassium mercuric iodide (see United States Pharmacopœia, page 529), *Marme's reagent*, a solution of potassium cadmium iodide, *Dragendorff's reagent*, a solution of potassium bismuth iodide, *Scheibler's reagent*, phosphotungstic acid, *Sonnenschein's reagent*, phosphomolybdic acid, *Wagner's reagent*, a

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solution of iodine together with potassium iodide, and others. The precipitates caused by these reagents in alkaloidal solutions are in some cases analogous to compounds formed in solutions of the inorganic bases, thus the alkaloidal periodides closely resemble potassium triiodide in composition, with the exception that some alkaloids have the power to combine with three, four, or even eight atoms of iodine. Many alkaloids give characteristic color reactions with acids and other reagents, by means of which their identity may be established; some of these reactions will be mentioned further on, in connection with the individual alkaloids. Very complete information regarding the behavior of alkaloids toward reagents as well as their source, solubilities, etc., is to be found in Sohn's *Dictionary of the Active Principles of Plants* (1894).

Until about 15 or 20 years ago comparatively little was known regarding the chemical constitution of alkaloids and their relation to each other. Since then numerous investigations have been actively carried on along these lines, and much valuable information has been published.[1] Such investigations will eventually lead to the successful synthetic production of numerous natural alkaloids, as is already the case, on a commercial scale, with cocaine and codeine.

The following natural alkaloids are recognized in the Pharmacopœia in an uncombined state: *Aconitine, Atropine, Cocaine, Codeine, Colchicine, Hydrastine, Morphine, Quinine, Strychnine*, and *Veratrine. Caffeine*, although possessing but very feeble basic properties, must nevertheless also be placed in this class; by some authorities it is not considered an alkaloid at all, since it is not precipitated by potassium mercuric iodide solution and other class reagents.

Salts of the following natural alkaloids are officially recognized: Atropine, Cinchonidine, Cinchonine, Cocaine, Codeine, Hyoscine, Hyoscyamine, Morphine, Pelletierine, Physostigmine or Eserine, Pilocarpine, Quinine, Scopolamine, Sparteine, and Strychnine; also salts of the following alkaloidal derivatives: Apomorphine, Hydrastinine.

THE OFFICIAL ALKALOIDS AND ALKALOIDAL SALTS.

Aconitine, $C_{34}H_{47}NO_{11}$.—This very poisonous alkaloid is found in the root of aconitum napellus, where it exists in combination with aconitic acid to an extent varying from 0.5 to 1.15 per cent. It is usually extracted by means of alcohol containing about ½ per cent. of tartaric acid. The alcoholic tincture is concentrated at a low temperature, mixed with water, and afterward with ether or petroleum benzin to remove fatty matter and resin, and finally precipitated by an excess of potassium or sodium carbonate. Amorphous bases are kept in solution by the alkaline liquid, and the washed precipitate is dissolved in ether and allowed to crystallize. By recrystallization from alcohol the alkaloid is eventually obtained pure.

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[1] The excellent work of Guareschi, translated from the Italian by Kunz-Krause, 2 vols., 1896 and 1897, and the more recent works by Pictet, translated from the French by Wolffenstein, and by Brühl, Hjelt, and Aschan, 1900, offer a very comprehensive compilation of everything pertaining to plant alkaloids up to very recent times. Unfortunately, these books have not yet been translated into English, and are accessible only to those familiar with the German language.

Commercial aconitine still occurs in both the amorphous and crystalline forms, but only the latter variety should be used, as the amorphous product contains derivatives considerably less active (10 or 15 times) than the crystallized alkaloid. The formula adopted by the Pharmacopœia for aconitine is that proposed by Freund and Beck in 1895, whereas the British Pharmacopœia assigns to the alkaloid the formula $C_{33}H_{43}NO_{11}$, suggested by Dunstan and Ince in 1891.

Aconitine melts, when rapidly heated, at 195° C. (383° F.), but if slowly heated it decomposes and melts at 182° C. (359.6° F.). It is very sparingly soluble in water and petroleum benzin, but dissolves readily in alcohol, ether, benzene, and chloroform. Sulphuric acid is without effect on aconitine, but if a crystal of ammonium vanadate be added, an orange color is produced. Aconitine may be distinguished from atropine and picraconitine by not yielding a violet color if a very small quantity be heated with a few drops of fuming nitric acid to dryness and the residue, when cool, then treated with alcoholic solution of potassium hydroxide.

It is used chiefly for the preparation of a 2 per cent. oleate, but is occasionally also prescribed for internal use. It must be handled with great care, the average adult dose being about 0.00015 Gm. or about $\frac{1}{410}$ grain.

Apomorphine Hydrochloride. $\mathbf{C_{17}H_{17}NO_2HCl}$.—Apomorphine may be classed among the so-called artificial alkaloids, being obtained by the action of hydrochloric acid on morphine or codeine. The process consists in heating either alkaloid with about 20 parts of pure hydrochloric acid in a sealed tube for several hours in an oil-bath to between 140° and 150° C. (284° and 302° F.). After cooling the liquid contained in the tube is diluted with water, when, upon the addition of an excess of sodium bicarbonate, apomorphine will be precipitated; the mixture is filtered and the new alkaloid extracted from the residue by means of ether or chloroform. The reaction occurring in the case of morphine appears to be simply an abstraction of the elements of water; thus, $C_{17}H_{19}NO_3 - H_2O = C_{17}H_{17}NO_2$; in the case of codeine, however, an intermediate product, chlorocodid, is formed, which is further split up into methyl chloride and apomorphine, thus, $C_{18}H_{21}NO_3 + HCl = C_{18}H_{20}ClNO_2 + H_2O$; $C_{18}H_{20}ClNO_2 = C_{17}H_{17}NO_2 + CH_3Cl$. If a few drops of hydrochloric acid be added to the ethereal or chloroformic solution above mentioned, apomorphine hydrochloride will separate in a crystalline form, and may be recrystallized from boiling water. The salt must be thoroughly dried over sulphuric acid and carefully protected against moisture, air, and light, otherwise it soon assumes a green color, due to oxidation.

Apomorphine hydrochloride is always dispensed in the form of aqueous solutions, and amber vials should be used for the same; the gradual green coloration of the solution can be prevented by addition of a few drops of hydrochloric or acetic acid. A solution of this salt may be readily distinguished from one of morphine hydrochloride by being colored red by addition of dilute ferric chloride solution, whereas the morphine solution will be colored blue. Apomorphine hydrochloride may also be distinguished from codeine, morphine, narceine, and narcotine by adding 0.05 Gm. of the salt to a solution of 0.05 Gm. of ferrous sulphate in 10 Cc. of water, when the solution will gradually turn blue and then black; addition of alcohol restores the blue color.

Atropine. $C_{17}H_{23}NO_3$.—This alkaloid belongs to the class known as mydriatic alkaloids, so named on account of their property of causing dilatation of the pupil of the eye, which occur in belladonna, duboisia, hyoscyamus, scopola, and stramonium, and include atropine, belladonnine, hyoscine, and hyoscyamine; daturine and duboisine, formerly considered as distinct alkaloids, are now known to be identical with atropine and hyoscyamine respectively. Atropine, and hyoscyamine have the same percentage composition, and the last named can be converted into the first by the action of alkalies in alcoholic solution. All three alkaloids are easily decomposed by strong acids and alkalies.

Atropine is found chiefly in belladonna, being obtained preferably from the root, as the latter is richer in alkaloid and free from chlorophyll. The finely powdered root is exhausted with alcohol, and the percolate mixed with calcium hydroxide to decompose the natural salt of atropine and liberate the alkaloid, which remains in solution; after filtration, the filtrate is acidulated with diluted sulphuric acid, concentrated to remove alcohol, fat, and resin, and treated with alkali carbonate in excess. The precipitated atropine is removed, washed with water, and dissolved in alcohol; to this alcoholic solution water is added, drop by drop, to incipient turbidity, and the alkaloid allowed to crystallize. Other bases present remain in the mother-liquor, but small quantities of hyoscyamine always accompany the commercial article.

Atropine is a monacid base possessing marked alkaline properties; it is capable of decomposing mercuric and mercurous chloride with the formation of the respective oxides; it also reddens phenolphtalein paper and restores the blue color of reddened litmus.

Commercial atropine is usually contaminated with small quantities of hyoscyamine, from which it is freed with difficulty and which has the effect of lowering the melting-point of the alkaloid. Pure atropine melts at 115.8° C. (240.4° F.), but the commercial product usually melts at 113.8° C. (236.8° F.), which is caused by the presence of hyoscyamine having a melting-point of 108° C. (226.4° F.).

The alkaloid atropine is very rarely used, except for the preparation of the official atropine oleate, a 2 per cent. solution.

Atropine Sulphate. $(C_{17}H_{23}NO_3)_2H_2SO_4$.—This salt may be prepared either by adding atropine slowly to a mixture of sulphuric acid and alcohol or by dissolving atropine mixed with water by means of diluted sulphuric acid. In either case a perfectly neutral solution must be obtained, which is then evaporated to dryness, at a temperature below 40° C. (104° F.). Some of the commercial salts show an acid reaction when dissolved in water, and are, therefore, unfit for use.

Caffeine, $C_8H_{10}N_4O_2 + H_2O$ **or** $C_5H(CH_3)_3N_4O_2 + H_2O$.—This feebly basic substance occurs in a number of plants belonging to different natural orders; thus, in coffee, tea, kola, and paullinia, associated with tannin, and varies in amount from less than 1 to 5 per cent. of the dried material. For commercial purposes it is usually obtained from powdered coffee-beans, not roasted, or preferably the fine, unsalable particles of tea leaves (tea leaves being also much richer in caffeine), by exhausting the same with hot water, adding a solution of lead acetate in slight excess, whereby tannin and coloring matters are precipitated, filtering, adding ammonia water to remove excess of lead salt, and again filtering. The filtrate is concentrated, hydrogen sulphide added to remove any lead still remaining, filtered, and further evaporated to the crystallizing-point. Milk of lime is also sometimes used to remove tannin, fat, coloring matter, etc., and is added to the powdered material, the mixture being then exhausted with warm 80 per cent. alcohol; the percolate is diluted with about one-sixth its volume of water and distilled to recover the alcohol. The aqueous residue is filtered and crystallized. If necessary, the product is redissolved, filtered through bone-black, and again crystallized.

Caffeine is very soluble in boiling water, 2 parts, and also in chloroform, 8 parts, but requires about 46 parts of water for solution at 25° C. (77° F.), which quantity is very materially reduced, however, by the presence of certain other substances, such as sodium benzoate, bromide, salicylate, and cinnamate, and even antipyrine.

The caffeine derived from different sources is identical, although the names theine and guaranine are still occasionally used. Considerable quantities of caffeine are now made synthetically in this country, but the process of manufacture is kept secret.

Caffeine is a derivative of xanthine, as shown by the murexide reaction mentioned below, being known as trimethyl xanthine, $C_5H(CH_3)_3N_4O_2$, and sometimes also called methyl-theobromine. It has been prepared synthetically by the action of methyl iodide on theobromine, $C_5H_2(CH_3)_2N_4O_2$, a basic substance found in cacao beans.

When treated with chlorine water or hydrochloric acid and potassium chlorate, as directed in the Pharmacopœia, caffeine yields, upon evaporation to dryness, a substance known as *amalic acid*, which, in the presence of air and ammonia, forms murexoin or tetramethyl murexide, $C_8(CH_3)_4N_5O_6(NH_4)$, of a rich purple color; this test is characteristic of caffeine and theobromine.

Under the name *citrated caffeine* (caffeina citrata), the Pharmacopœia recognizes an intimate mixture, by some declared to be a definite, but feeble, chemical compound, obtained by dissolving 50 Gm. of caffeine in a solution of 50 Gm. of citric acid and 100 Cc. of hot water, and evaporating the solution to dryness on a water-bath, with constant stirring. The resulting product is a white powder with acid taste and reaction. With 3 parts of water it forms a clear, syrupy liquid, from which caffeine is precipitated upon addition of 5 parts of water; when 25 parts of water have been added, however, the precipitate is redissolved. The presence of tartaric acid may be determined by the development of a brown or black color, if 0.25 Gm. of the powder be heated with 5 Cc. of sulphuric acid for 5 minutes on a water-bath.

The Pharmacopœia also directs the preparation of effervescent citrated caffeine to contain 4 per cent. of the salt; this preparation is made according to the general directions for granular effervescent salts, and has been considered on pages 409 and 410.

Cinchonidine Sulphate. $(C_{19}H_{22}N_2O)_2H_2SO_4 + 3H_2O$.—Cinchonidine is one of the four important alkaloids found, among a large number (32), in cinchona bark, and occurs in greater proportion in the so-called red bark, derived from cinchona succirubra, than in others. The sulphate is obtained from the mother-liquors left in the manufacture of quinine sulphate, and is purified by fractional crystallization. The official salt, containing but three molecules, 7.29+ per cent., of water of crystallization, is the result of using a hot, concentrated solution, for if the salt be crystallized from weaker solutions it will contain six molecules, or 14.6 per cent. of water.

Absolute purity of the commercial salt is not practicable, nor demanded by the Pharmacopœia, hence a slight fluorescence is sometimes observed in solutions of the salt made with diluted sulphuric acid. The official test with Rochelle salt and ammonia water depends upon the insolubility of cinchonidine tartrate, the tartrates of cinchonine and quinidine being dissolved and reprecipitated upon addition of ammonia.

Cinchonidine Salicylate. $C_{19}H_{22}N_2O.HC_7H_5O_3$.—This salt, although not officially recognized, has been used extensively by physicians, and may be prepared by direct union of the alkaloid and acid. A neutral solution should be made in hot water or diluted alcohol and allowed to crystallize upon cooling; the salt is sparingly soluble in cold water.

Cinchonine Sulphate, $(C_{19}H_{22}N_2O)_2H_2SO_4 + 2H_2O$.—The usual process for making this salt is to dissolve the alkaloid cinchonine in warm diluted sulphuric acid until the acid is neutralized and then concentrate and crystallize the solution. The Pharmacopœia requires the absence of more than 5 per cent. of water of crystallization. Cinchonine sulphate may be readily distinguished from cinchonidine sulphate by its greater solubility in chloroform, requiring not over 69 parts for solution, while the latter requires about 900 parts at 25° C. (77° F.).

Cocaine, $C_{17}H_{21}NO_4$ or $C_8H_{13}(C_6H_5CO)NO.COOCH_3$.—The leaves of Erythroxylon Coca contain a number of basic principles, all derivatives of ecgonine, $C_9H_{15}NO_3$, of which cocaine is the most important; other non-crystallizable bases are truxilline or isatropylcocaine (known also as cocamine), $C_{19}H_{23}NO_4$, hygrine, $C_{12}H_{13}N$, and cinnamylcocaine, $C_{19}H_{23}NO_4$. Cocaine appears in the plant united with coca-tannic acid. The processes employed for the isolation of cocaine are usually guarded as secrets by manufacturers, and it is known that large quantities of the alkaloid are now prepared synthetically, owing to the difficulty of extracting *pure* cocaine in remunerative quantities from the drug.

When finely powdered coca leaves are moistened with solution of sodium hydroxide and then treated with petroleum ether, kerosene, or gasolin, the alkaloids present are liberated and taken up by the menstruum, from which they can be transferred, as salts, to diluted sulphuric acid, through intimate contact by agitation. If to this acid solution solution of soda be added in excess, cocaine mixed with some of the lesser alkaloids will be precipitated, the bulk of the hygrine, however, remaining in solution; the crude cocaine may be removed by filtration and expression and purified by crystallization from alcohol. As the yield of cocaine is known to decrease materially by transportation, no doubt owing to decomposition, the result of fermentation in the imperfectly dried and tightly packed leaves, the bulk of the natural alkaloid is now manufactured in South America, in places adjacent to the source of gathering the leaves, processes of extraction very similar to the above being employed.

In order to avoid loss of the decomposition-products and other alkaloids accompanying cocaine in the crude article, the pure alkaloid is now extensively prepared by synthesis, in the following manner, which is possible, since the chemical constitution of cocaine is definitely known to be methyl-benzoyl-ecgonine. Boiling the mixed bases with hydrochloric acid converts them all into ecgonine, $C_9H_{15}NO_3$, and if ecgonine hydrochloride, $C_9H_{15}NO_3HCl$, be dissolved in methyl alcohol and the solution treated with dry hydrochloric acid gas, hydrochloride of methyl-ecgonine, $C_9H_{14}CH_3NO_3HCl$, will be formed and can be crystallized from an alcoholic solution. By heating this latter compound with benzoyl chloride, C_6H_5COCl, ammonia, morphine will be precipitated, while codeine remains in solution and may be recovered by crystallization; if potassium or sodium hydroxide be used in place of ammonia, codeine will be precipitated, the morphine remaining in solution. Large quantities of codeine are now made synthetically from morphine by methylation, which is effected by allowing methyl iodide or chloride, or sodium methylsulphate, to act upon an alkaline solution of the latter alkaloid.

Codeine crystallizes from an aqueous solution with one molecule (5.67 per cent.) of water, which constitutes the official article; if crystallized from ether or carbon disulphide, it is anhydrous. Its crystals are larger than those of any other alkaloid and are soluble in 88 parts of water.

Chemically, codeine is closely allied to morphine, as shown by the formula, $C_{17}H_{18}CH_3NO_3$, which differs from that of morphine by a methyl group, hence the name methyl-morphine. It differs, however, from morphine in its behavior toward certain reagents and may be readily distinguished from that alkaloid by the tests given in the Pharmacopœia. When heated with strong hydrochloric acid, in a sealed tube, both alkaloids yield apomorphine, but, if heated to 180° C. (356° F.) with a concentrated solution of zinc chloride, codeine yields *apocodeine*, $C_{18}H_{19}NO_2$, whilst morphine again yields apomorphine. The name codeine is derived from the Greek word *κώδεια*, meaning head, referring to the source of the alkaloid, poppy heads.

Codeine Phosphate, $C_{18}H_{21}NO_3H_3PO_4 + 2H_2O$.—This salt may be obtained by dissolving the alkaloid codeine in a mixture of phosphoric acid and water, and precipitating the newly formed compound by addition of alcohol; it may then be recrystallized after solution in hot water. The quantity of water of crystallization taken up by the salt is not uniform, thus, while the official salt of our Pharmacopœia contains 2 molecules or 8.32 per cent. of water, that of the British Pharmacopœia contains but 6.37 per cent.

Codeine phosphate is soluble in less than 2½ times its weight of water, forming an acid solution. It represents 65 per cent. of its weight of codeine, and responds to all the tests given in the Pharmacopœia for that alkaloid.

Codeine Sulphate, $(C_{18}H_{21}NO_3)_2H_2SO_4 + 5H_2O$.—If codeine be dissolved in warm water, the solution exactly neutralized by addition of diluted sulphuric acid, and then concentrated by evaporation and set aside, codeine sulphate of the above composition, containing about 11.5 per cent. of water, will crystallize out. The salt contains about 76 per cent. of codeine and is far less soluble than codeine phosphate, but yields a neutral solution, requiring 30 times its weight of water at 25° C. (77° F.).

Colchicine, $C_{22}H_{25}NO_6$ or $C_{15}H_{10}.(OCH_3)_3.NHCOCH_3.COOCH_2$.—Although colchicine was discovered in 1820, its true chemical nature was not determined until nearly seventy years later.

The pure alkaloid may be prepared by the following process, which is based upon the fact that it is capable of forming a crystalline compound with chloroform: Colchicum seed are exhausted with hot 90 per cent. alcohol, the alcohol recovered by distillation, the residue treated with water equal in quantity to $\frac{1}{5}$ of the weight of the drug used, and filtered for the removal of resin, wax, and fatty matter. The clear, dark-brown filtrate is well shaken with four successive portions of chloroform, which are united and distilled, the residue being again dissolved in water and shaken with chloroform. From the latter solution crude colchicine-chloroform separates upon evaporation of the solvent and is dissolved in alcohol, the solution being again concentrated by distillation. A third treatment with chloroform yields a yellow solution, which is evaporated on a water-bath, and the residue treated with lukewarm ether and set aside, when pure colchicine chloroform, having the composition $C_{22}H_{25}NO_6.2CHCl_3$, will separate in the form of faintly yellowish needle-shaped crystals, which are decomposed in the presence of water when heated to 100° C. (212° F.), the chloroform escaping and leaving pure colchicine in aqueous solution, from which it may be obtained as an amorphous mass by evaporation to dryness or in form of lamellæ by spreading the concentrated solution on plates of glass and drying.

Colchicine is more soluble in water than any other alkaloid, requiring but 22 parts at 25° C. (77° F.).

The salts of colchicine are not very stable. The one most used is the salicylate, $C_{22}H_{25}NO_6.HC_7H_5O_3$, made by moistening a mixture of 20 parts of colchicine and 7 parts of salicylic acid with water and subsequently drying the same. It is a yellow amorphous powder, soluble in water and alcohol.

The name *colchisal* has been given to a solution of colchicine in methyl salicylate, dispensed in gelatin capsules, each containing 0.00025 Gm. of the alkaloid and 0.2 Gm. of the methyl ester.

Homatropine Hydrobromide, $C_{16}H_{21}NO_3HBr$.—This salt, which resembles atropine in its physiological effects, is obtained by heating a concentrated neutral solution of tropine mandelate for several days on a water-bath with about half its volume of 12 per cent. hydrochloric acid. A part of the tropine mandelate remains intact and a part yields homatropine, which combines with the hydrochloric acid, forming a salt, which is subsequently decomposed with ammonia water and the liberated alkaloid extracted with chloroform. The chloroformic solution is freed from water with anhydrous potassium carbonate, and then distilled, yielding a syrupy liquid, which congeals to a crystalline mass, and may be exactly neutralized with diluted hydrobromic acid. The salt thus formed may be further purified by repeated crystallization from alcoholic solution. Homatropine hydrobromide may be distinguished from atropine by treating with fuming nitric acid, evaporating the mixture to dryness, and adding to the residue some freshly prepared alcoholic solution of potassium hydroxide, when homatropine gives a reddish-yellow color, while atropine causes a violet color. Another test depends upon the fact that while atropine and hyoscyamine hydrobromides are soluble in all proportions in chloroform, the homatropine salt is very sparingly soluble in that liquid. The melting-point of the pure alkaloid homatropine, obtained by means of solution of sodium hydroxide and extraction with ether, is 19 degrees lower than that of atropine and 12 degrees lower than that of hyoscyamine, being only 96° C. (204.8° F.). The mydriatic effects of homatropine salts are of far shorter duration than those of atropine, and a solution instilled into the eye does not cause dryness of the throat and fauces, as in the case of atropine salts. The hydrochloride, sulphate, and salicylate of homatropine have also been used.

Hydrastine. $C_{21}H_{21}NO_6$.—This body must not be confounded with the mixture of resinoid substances sold under a similar name, hydrastin. The alkaloid, hydrastine, occurs in the root of hydrastis canadensis, golden seal, associated with berberine, and in commerce is frequently designated as the white alkaloid of hydrastis. Exactly how hydrastine exists in the drug was, for a long time, uncertain, some authorities contending that it is combined with an acid, and others that it exists free. According to investigations by Dohme and Engelhardt (1895), a portion of the alkaloid, about 20 per cent. of the total yield, exists in a free state, the remainder being in combination with an acid, the nature of which has not yet been determined. While formerly supposed to be present only in small proportions, hydrastine has been shown to occur frequently to the extent of 2.33 per cent. in the fresh or 3.14 per cent. in the dried root.

In extracting hydrastine for commercial purposes it becomes necessary first to remove the berberine. This is best done by adding a large excess of sulphuric acid to an alcoholic tincture of hydrastis root; after three or four hours a mass of crystals of berberine sulphate will have separated, and to the supernatant liquid, after filtration, ammonia water is added until the liquid is but slightly acid. Having removed the accumulated ammonium sulphate by straining, the liquid is concentrated to a syrupy consistence and poured into ten times its bulk of cold water, whereby fat and resinous matter are precipitated. To the solution of crude hydrastine sulphate separated by filtration, ammonia water is then added in excess and the impure hydrastine collected, which may be purified by resolution in diluted sulphuric acid, reprecipitation by ammonia, and repeated crystallization from alcohol.

Hydrastine is a weak base, melting at 135° C. (275° F.), which, while readily soluble in acidulated water, forms difficultly crystallizable salts. It may be distinguished from hydrastinine by the blue fluorescence developed when a crystal of the alkaloid is dissolved in diluted sulphuric acid and a 10 per cent. solution of potassium permanganate then added. Hydrastine is extensively used in preparing the so-called "colorless hydrastis," which is a solution of the alkaloid in a mixture of water and glycerin with the aid of hydrochloric or sulphuric acid.

Hydrastinine Hydrochloride, $C_{11}H_{11}NO_2HCl$.—The alkaloid hydrastinine does not occur in any plant, but is an artificial base obtained by oxidation of hydrastine—the white alkaloid found in hydrastis—by means of nitric acid. The mixture of hydrastine and nitric acid is moderately heated to 50° or 60° C. (122° to 140° F.) until ammonia water no longer causes precipitation. The reaction taking place produces hydrastinine and opianic acid, the latter crystallizing out on cooling of the solution, while hydrastinine is subsequently precipitated in crystalline form upon supersaturation of the filtrate with solution of potassium hydroxide.

Although hydrastinine hydrochloride is of light-yellowish or yellowish-white color, pure white alkaloid will separate after some time from a solution of 0.2 Gm. of the salt in 3 Cc. of water to which 4 or 5 drops of a 15 per cent. solution of sodium hydroxide have been added slowly, the mixture being shaken after each addition.

The salt is very soluble in water and alcohol; its aqueous solution is not precipitated by addition of ammonia water, differing in this respect from the salts of hydrastine.

Hyoscine Hydrobromide, $C_{17}H_{21}NO_4HBr + 3H_2O$.—Hyoscine is an amorphous alkaloid, occurring in the plants belonging to the natural order of the Solanaceæ, associated with hyoscyamine and atropine. It is found in largest quantity, about $\frac{1}{50}$ or $\frac{1}{30}$ per cent., in the seed of hyoscyamus and the leaves of the duboisia. For commercial purposes hyoscine is obtained from either of the above sources, chiefly henbane seed, by exhausting the drug with 80 per cent. alcohol, recovering the alcohol by distillation, and setting the residue aside for several days, when a fatty layer separates from the aqueous solution of the mixed bases in combination with organic acids. By addition of alkali carbonate to the aqueous solution, the alkaloids are liberated and may be abstracted by agitation with ether. Upon evaporation of the ether a syrupy liquid is obtained, from which nearly all the hyoscyamine present crystallizes out; the hyoscine may be isolated from the mother-liquor by converting it into an aurochloride, separating the same by fractional crystallization, redissolving in water, and, after removal of the gold by means of hydrogen sulphide, precipitating the hyoscine from the filtrate, by alkali carbonate, in the form of an oily layer, which may be purified by solution in chloroform and evaporation of the solvent. Hyoscine usually occurs as an amorphous mass, but when perfectly pure crystallizes in prisms which melt at 59° C. (138.2° F.).

The official salt may be obtained by dissolving hyoscine in a very slight excess of diluted hydrobromic acid, concentrating the solution, and allowing it to crystallize. It contains about 12.5 per cent. of water.

Hyoscine is chemically indentical with the alkaloids *duboisine*, obtained from duboisia myoporoides, and *scopolamine*, obtained from several varieties of scopola; it also occurs in belladonna and stramonium. Although the title hyoscine hydrobromide is still recognized in the United States and British Pharmacopœias, the German Pharmacopœia has adopted in its stead the title scopolamine hydrobromide for this salt, which latter is used as a synonym in the British Pharmacopœia. The salt scopolamine hydrobromide is separately recognized in our own Pharmacopœia, but accompanied by the statement that the salt is chemically identical with hyoscine hydrobromide. Recent published statements make it appear as if commercial scopolamine may be a mixture and, after all, not identical with hyoscine.

Hyoscyamine Hydrobromide, $C_{17}H_{23}NO_3HBr$.—The alkaloid hyoscyamine was discovered about 1833 and is officially recognized in the French Pharmacopœia. It is an isomer of atropine, being readily converted into the same, and is easily altered by alkalies and contact with heat, hence all manipulation and heating must be reduced to a minimum during its isolation. Hyoscyamine may be obtained from the mother-liquors left after the manufacture of atropine, or direct from henbane seed, as outlined in the extraction of hyoscine, or as follows: Hyoscyamus seed having been freed from fatty matter by treatment with petroleum benzin and dried are exhausted with 85 per cent. alcohol. The tincture after acidulation with hydrochloric acid is concentrated in a vacuum apparatus and filtered, the filtrate being again treated with petroleum benzin and then rendered alkaline with potassium carbonate, after which it is shaken out with chloroform. Upon evaporation of the chloroformic solution at a low temperature, the hyoscyamine is obtained as a gummy mass and may be purified by solution in dilute sulphuric acid, filtering, and crystallizing. From the sulphate thus obtained, the alkaloid is liberated by making an aqueous solution alkaline and extracting with chloroform, which then yields hyoscyamine upon evaporation. Although crystallizable, hyoscyamine usually occurs in commerce in an amorphous condition. The exact relation between hyoscyamine and atropine was revealed in 1902 by Amenomiya, a Japanese chemist, who succeeded in converting atropine into dextro- and lævorotatory hyoscyamine; further details of this subject may be found in the *National Standard Dispensatory*, page 796.

Hyoscyamine hydrobromide may be prepared by dissolving 10 parts of the alkaloid in 11 parts of 25 per cent. hydrobromic acid, concentrating the solution, and crystallizing. It occurs both in the chloride occurs in large masses of feathery crystals, and is more bulky, weight for weight, than the sulphate. It can be rendered perfectly anhydrous at a temperature of 100° C. (212° F.).

Morphine Sulphate. $(C_{17}H_{19}NO_3)_2H_2SO_4 + 5H_2O$. — Next to quinine sulphate there is probably no alkaloidal salt more extensively used by physicians than this one, and, unfortunately, its unauthorized use among the laity is on the increase in this country, owing to the lack of sufficient legal restrictions and the cupidity of certain pharmacists and dealers in drugs. Like the two preceding salts, morphine sulphate is made from the alkaloid by dissolving the same in sufficient diluted sulphuric acid to form a neutral solution and setting this aside to crystallize. The official salt contains 11.87 per cent. of water of crystallization, of which, however, only a part, 7.12 per cent., can be expelled at the temperature of a boiling-water bath.

An aqueous solution of morphine sulphate is largely used in some parts of this country under the name *Magendie's Solution ;* it contains 16 grains of the salt in each fluidounce, which is equal to about $\frac{1}{30}$ of a grain in each minim. As aqueous solutions of morphine sulphate do not keep well for any length of time, one-half grain of salicylic acid has been used in each fluidounce of this solution with excellent results. Prior to 1880, a solution of morphine sulphate was officially recognized in the Pharmacopœia; this solution contained only one grain of the salt in each fluidounce, and must not be confounded with Magendie's solution.

Of the unofficial salts of morphine the hydrobromide, citrate, meconate, phthalate, tartrate, and valerate have been employed. Morphine tartrate, $(C_{17}H_{19}NO_3)_2C_4H_6O_6 + 3H_2O$, is official in the British Pharmacopœia, which authority also recognizes a solution of the salt containing 0.010 Gm. in 1 Cc. or 1 grain in 110 minims.

Pelletierine Tannate.—Under this title the Pharmacopœia recognizes a mixture in varying proportions of the tannates of four alkaloids obtained from the bark of pomegranate. The four alkaloids are pelletierine, isopelletierine, methylpelletierine, and pseudopelletierine, also known as punicine, isopunicine, methylpunicine, and pseudopunicine, the former names being preferred and given in honor of the French chemist, Pelletier.

To obtain the mixture of alkaloids designated as pelletierine tannate, the ground bark is mixed with milk of lime, transferred to a percolator, and exhausted with water. The resulting infusion is shaken out with chloroform, and the chloroformic solution of free alkaloids then shaken out with very dilute sulphuric acid. If to a neutral solution of the mixed sulphates a solution of tannic acid be added, the sparingly soluble tannates will be precipitated and are subsequently dried.

Commercial pelletierine tannate occurs as a light-yellow, odorless, amorphous powder, possessing an astringent taste and a weak acid reaction. It contains a small amount, about 7 per cent., of moisture and requires about 235 parts of water for solution. Being a mixture of alkaloidal tannates, no formula can be given for its composition. Pure pelletierine, $C_8H_{15}NO$, which can be extracted from the above mixture, is a colorless, volatile liquid, having strong basic properties and forming crystallizable salts with acids. It is soluble in 23 parts of water and when exposed to air undergoes oxidation and turns dark.

Physostigmine Salicylate or Eserine Salicylate, $C_{15}H_{21}N_3O_2$-$C_7H_6O_3$.—The alkaloid physostigmine occurs in calabar beans to the extent of rarely more than one-sixth of 1 per cent., and its isolation requires considerable care, owing to its ready decomposition. The usual method of extraction is to exhaust the powdered bean with 85 per cent. alcohol and concentrate the tincture in a vacuum apparatus to a syrupy consistence; the resulting extract separates into an upper layer, consisting of fat, etc., and a lower, aqueous solution of the natural salts of the alkaloids. By treating the aqueous layer with sodium bicarbonate, and then repeatedly shaking with ether, the liberated physostigmine may be extracted; the ethereal solution is next treated with diluted sulphuric acid, so as to obtain a solution of the alkaloid as sulphate, leaving impurities, fat, resin, etc., in the ethereal liquid. The pure alkaloid is finally obtained by decomposing the sulphate with sodium bicarbonate, extracting again with ether and crystallizing. Heat must be avoided as far as possible, also the use of strong alkalies, as in the case of the mydriatic and other easily decomposable alkaloids.

Physostigmine salicylate may be prepared by neutralizing a solution of the alkaloid in absolute alcohol with pure salicylic acid; the salt gradually separates in needle-shaped crystals, free from color, which can be then drained and dried.

Some of the salts of physostigmine and their aqueous solutions readily assume a reddish color when exposed to light and air, hence they must be dispensed in tightly closed amber vials; the name rubereserine has been given to the red substance thus formed. The salicylate is less liable to change by exposure to light than the other salts; but, owing to its lesser solubility in water, is not as much used as the sulphate.

The name *eserine*, by which physostigmine is also known, was derived from the word *esère*, meaning split nut, the name applied by the African negroes to the calabar bean. Calabarine is the name given to another alkaloid present in the bean, which, however, is insoluble in ether.

Physostigmine Sulphate, $(C_{15}H_{21}N_3O_2)_2H_2SO_4$.—The preparation of this salt has already been indicated above in connection with the extraction of the alkaloid from the drug; by carefully neutralizing an alcoholic solution of physostigmine with sulphuric acid and concentrating the solution to a syrupy liquid, at moderate temperature, crystals of the salt may be obtained. The Pharmacopœia describes physostigmine sulphate as a white or yellowish-white crystalline powder, but the commercial article is rarely entirely free from color, generally occurring in yellowish, amorphous, very hygroscopic masses.

This and the preceding salt may be distinguished from each other by adding platinic chloride test-solution to an aqueous solution of the salt, when a yellowish-white precipitate will be formed in the case of the sulphate, but no precipitate at all in the case of the salicylate. Both salts are used, in the form of solution and gelatin disks, for the purpose of producing myosis or contraction of the pupil of the eye.

Pilocarpine Hydrochloride, $C_{11}H_{16}N_2O_2HCl$.—The pure alkaloid pilocarpine is recognized in the French Pharmacopœia and may be obtained by moistening finely ground pilocarpus leaves with a solution of sodium carbonate and extracting with warm benzene. The benzene solution is shaken out with diluted hydrochloric acid, and after separation the acid liquid is made alkaline with sodium carbonate and shaken out with chloroform. Upon evaporation of the chloroformic liquids a mixture of crude alkaloids results, which is neutralized by means of nitric acid, evaporated to dryness, and purified by repeated crystallization from alcohol. Finally, the pilocarpine nitrate is dissolved in water, the solution made alkaline with ammonia water, and shaken out with chloroform; the latter solution, upon evaporation, yields the pure alkaloid in the form of a colorless, strongly basic, syrupy liquid, soluble in water, alcohol, and chloroform, but scarcely soluble in ether.

Pilocarpine hydrochloride is made by neutralizing diluted hydrochloric acid with pure pilocarpine, concentrating the solution and setting the same aside to crystallize over sulphuric acid, or the solution may be evaporated to dryness, when the salt will be obtained as a crystalline powder. The salt is deliquescent on exposure to air and when triturated with an equal weight of calomel forms a black mixture. The Pharmacopœia mentions the following special test as characteristic of the salts of pilocarpine: Dissolve 0.01 to 0.02 Gm. of the salts in 2 Cc. of water in a test-tube, add 2 Cc. of a solution of hydrogen peroxide (slightly acid), and carefully pour on top of the liquid a small layer of benzene; then add 3 or 4 drops of a 0.3 per cent. solution of potassium dichromate and shake gently. The benzene layer will turn violet, while the aqueous layer will remain yellow. (If more than 0.02 Gm. is used, the benzene turns blue, and the reaction is no longer characteristic.)

The salts of pilocarpine are used chiefly as diaphoretics and sialogogues, but also possess decided myotic properties, like those of physostigmine.

Pilocarpine Nitrate, $C_{11}H_{16}N_2O_2.HNO_3$.—This salt may be obtained as described above in the manufacture of pure pilocarpine, or by neutralizing diluted nitric acid with the pure alkaloid. After a neutral solution has been secured, the same is slowly evaporated to dryness, redissolved in hot alcohol, and allowed to crystallize.

Pilocarpine nitrate differs from the hydrochloride in being permanent in the air and in not forming a black mixture when triturated with an equal weight of calomel. It responds to the special test mentioned in the preceding article.

Quinine. $C_{20}H_{24}N_2O_2+3H_2O$.—This is, no doubt, the most important and extensively used of all alkaloids. It occurs to a varying extent in the different species of cinchona, the yield having increased greatly with careful cultivation of the trees in India, Java, etc. The bases present in cinchona bark exist in combination with quinic or kinic, quinovic, and cinchotannic acids, and are usually extracted by means of acidulated water. The infusion is concentrated and mixed with milk of lime, whereby the alkaloids are liberated, while the calcium compounds of the organic acids are precipitated together with much coloring-matter. By straining the mixture and exhausting the residue repeatedly with boiling alcohol, amyl alcohol, petroleum benzin, or kerosene, a solution of the crude alkaloids is obtained, from which the latter may be transferred as sulphates by treatment with diluted sulphuric acid. Another plan is to mix the powdered bark with solution of sodium hydroxide or milk of lime, whereby the natural combinations are broken up and the alkaloids liberated; the mixture is then exhausted, in a suitable apparatus, with hot alcohol or kerosene, from which, after proper concentration, the alkaloids are extracted as acid sulphates by means of sulphuric acid.

In either case the acid solution is treated with animal charcoal, and the liquid, while hot, after filtration, neutralized with solution of sodium hydroxide, when, upon cooling, neutral quinine sulphate crystallizes out and may be purified by resolution, recrystallization, etc. The other alkaloids, including also small quantities of quinine sulphate, remain in the mother-liquor and may be recovered as stated elsewhere.

From the purified quinine sulphate the alkaloid may be obtained by precipitation with sodium hydroxide, or ammonia water in very slight excess, after solution of the salt in water with the aid of an acid.

Official quinine alkaloid contains about 14.3 per cent. of water of crystallization, and melts at a comparatively low temperature, 57° C. (134.6° F.); at 100° C. (212° F.) about two-thirds of the water is expelled, but it does not become anhydrous until a temperature of 125° C. (257° F.) is reached. The commercial article varies considerably in appearance and solubility, due, no doubt, to different methods of manufacture; some is crumbly, compact, and idio-electric, dissolving slowly in alcohol and even dilute acids, while alkaloid in ammonia water. As already stated under Quinine, the larger quantity of ammonia water allowed by the Pharmacopœia is made necessary in case the maceration of the salt is conducted at a higher temperature, because more of the salt will be taken up by the water. While not more than 6 Cc. of ammonia water is allowed for 0.5 Gm. of quinine sulphate, if macerated at 15° C. (59° F.) to produce a clear solution of the pure alkaloid, an increase of 0.5 Cc. is permitted for 1° C. (1.8° F.) increase in temperature during maceration. De Vrij and Schaefer have shown that a considerable percentage of lesser cinchoma alkaloids may escape detection by Kerner's test; hence the German Pharmacopœia has adopted a modification by Kerner and Weller, which consists in digesting in a test-tube 2 Gm. of quinine sulphate dried at 40° or 50° C. (104° or 122° F.) with 20 Cc. of distilled water at 60° or 65° C. (140° or 149° F.) for 30 minutes, with frequent agitation. The tube and contents are then cooled and kept at a temperature of 15° C. (59° F.) for two hours, with frequent agitation, after which the mixture is filtered; 5 Cc. of the filtrate should yield a clear solution with 4 Cc. of 10 per cent. ammonia water. This test is much more severe than that of the United States Pharmacopœia, and demands a much purer salt. Whenever solutions of alkaloidal salts are filtered it should be borne in mind that filter paper abstracts appreciable quantities of the salt from solution; it should, therefore, either be filtered through glass wool, or the filtrate through paper should be collected in fractions of 5 Cc. each, of which the second or third fraction only should be used for the above test.

Chemically pure quinine sulphate has been offered for sale for some time. This is obtained by first preparing pure quinine bisulphate by repeated recrystallization, and then exactly neutralizing a hot aqueous solution thereof with sodium carbonate, when, upon cooling, pure quinine sulphate will crystallize out.

The most convenient test for chemically pure quinine sulphate is either Schaefer's test with potassium oxalate or DeVrij's test with potassium chromate; both depend upon the very sparing solubility of the respective quinine salts. Schaefer's test is made as follows: 1 Gm. of official or 0.85 Gm. of anhydrous quinine sulphate is dissolved in 35 Cc. of distilled water by means of heat in a small flask previously tared; a solution of 0.3 Gm. of crystallized neutral potassium oxalate in 5 Cc. of water is then added, the contents of the flask made to weigh 41.3 Gm. by addition of distilled water, and the mixture kept at a temperature of 20° C. (68° F.) for thirty minutes, with occasional agitation.

After filtration one drop of solution of sodium hydroxide added to 10 Cc. of the filtrate should produce no turbidity within three or five minutes. Less than 1 per cent. of other cinchona alkaloids can be detected by this method.

Quinine sulphate can be crystallized with varying proportions of water, the official salt being allowed as much as 16.18 per cent. As the salt effloresces upon exposure, the symbolic formula given in the Pharmacopœia representing 14.43 + per cent. of water probably indicates the average composition of the commercial salt. Very appreciable loss of weight has been observed in cases where the salt was preserved in paper boxes, hence manufacturers use either glass or tightly sealed tin containers. It is the least soluble of the official quinine salts, requiring at 25° C. (77° F.) 720 parts of water, or 86 parts of alcohol, or 36 parts of glycerin. At 60° C. (140°F.) it loses all but 2 molecules of its water of crystallization, the remainder not being entirely expelled until a temperature of 115° C. (239° F.) is reached.

The emerald-green color mentioned in the Pharmacopœia as occurring when a dilute aqueous solution of the quinine sulphate is mixed with a little bromine water and an excess of ammonia water is due to the formation of a resinous body to which the name *thalleioquin* (from the Greek word *θάλλός*, a green branch) has been given. Chlorine water may be used in place of bromine water, but, according to Flückiger, the latter is more sensitive, detecting as little as 1 part of quinine in 20,000 of solution. The thalleioquin reaction is characteristic of quinine salts, but is also obtained with quinidine.

The following salts of quinine are not recognized in the Pharmacopœia, but are used to some extent by physicians, and are therefore mentioned here:

Quinine Tannate. $C_{20}H_{24}N_2O_2(C_{14}H_{10}O_9)_2$.—Although tannic acid is known to precipitate quinine from a neutral solution of its salts in water, this compound is intentionally used by physicians on account of its very sparing solubility, which renders its bitter taste less perceptible. The salt is usually prepared by adding a solution of 1.8 parts of tannic acid in 18 parts of water to a solution of 1 part of quinine sulphate in 30 parts of water, made with just sufficient sulphuric, or preferably acetic, acid. Any excess of acid is carefully neutralized with ammonia, and the precipitate allowed to subside, then washed on a filter with water, being afterward dried at a very moderate heat. Quinine tannate is officially recognized in the German Pharmacopœia.

Quinine Valerate. $C_{20}H_{24}N_2O_2.HC_5H_9O_2 + H_2O$.—This salt may be conveniently prepared by dissolving freshly precipitated quinine alkaloid in warm water by means of valeric acid and crystallizing the solution upon cooling. It is decomposed at the temperature of boiling water, losing valeric acid.

Scopolamine Hydrobromide. $C_{17}H_{21}NO_4HBr + 3H_2O$.—As already stated under Hyoscine Hydrobromide, the Pharmacopœia considers the two salts as chemically identical. Although the name was given to the alkaloid because first found in scopola root, for commerical purposes it is probably made from henbane seed by the method given on page 734 for the manufacture of hyoscine hydrobromide. Its properties and reactions are the same as those of the latter salt.

Sparteine Sulphate. $\mathbf{C_{15}H_{26}N_2H_2SO_4 + 5H_2O}$.—Sparteine is the only alkaloid belonging to the class of amines recognized in the Pharmacopœia. It is a liquid heavier than water, and has been obtained by extracting scoparius with water acidulated with sulphuric acid, concentrating the infusion, decomposing the salt with sodium hydroxide, and distilling. The distillate is supersaturated with hydrochloric acid, evaporated to dryness, and distilled with the aid of potassium hydroxide; first ammonia passes over, after which sparteine distils and condenses as a thick, oily liquid. Another method consists in exhausting the powdered drug with 60 per cent. alcohol, evaporating the tincture at a low temperature, and extracting the alkaloid with the aid of tartaric acid; the solution of sparteine tartrate is then decomposed with potassium carbonate, and the alkaloid thus liberated abstracted with ether. Pure sparteine is a colorless fluid, boiling at 287° C. (548.6° F.) and having an aniline-like odor and intensely bitter taste. It is easily decomposed upon exposure to air and light.

Sparteine sulphate is prepared by neutralizing the purified alkaloid with diluted sulphuric acid and rapidly concentrating the solution, when colorless crystals will be obtained. As indicated by the official formula, it is the salt of a diacid base. The Pharmacopœia recognizes the presence of 5 molecules (21.34 per cent.) of water of crystallization, which compound is obtained by recrystallizing the salt from diluted alcohol. Sparteine sulphate crystallizes with different proportions of water under varying conditions, and also occurs in the form of an anhydrous salt. It is hygroscopic and is soluble in a little more than its own weight of water, yielding a solution having an acid reaction toward litmus.

Strychnine. $\mathbf{C_{21}H_{22}N_2O_2}$.—This alkaloid occurs in combination with an acid to which formerly the name igasuric acid was given, but which has been shown to be a variety of tannic acid, similar to caffeotannic acid. It is generally associated with brucine, in the seed of strychnos nux vomica and other members of the natural order Loganiaceæ. The proportion of strychnine present in the seed varies, sometimes reaching as high as 1.8 per cent.

To extract the alkaloids the powdered drug may be exhausted with boiling water acidulated with hydrochloric or sulphuric acid, whereby the alkaloids are obtained in solution as hydrochlorides or sulphates. Upon concentration of the infusion and addition of milk of lime the alkaloids are precipitated, and by collecting upon a strainer and washing the residue with water much foreign matter is removed.

Subsequent treatment of the residue with cold diluted alcohol removes brucine, the treatment being continued as long as the washings are reddened by nitric acid, after which boiling alcohol is used to extract the strychnine; this, after recovery of the alcohol, is converted into sulphate by solution in diluted sulphuric acid, filtered through animal charcoal, and precipitated with an alkali.

Some manufacturers exhaust the drug with hot alcohol of about 60 per cent., concentrate the tincture, filter, and add lead acetate, whereby the tannic acid is removed together with coloring-matters, while the alkaloids remain in solution as acetates. After a second filtration the alkaloids are precipitated by ammonia, and may be further treated as above or dissolved in hot alcohol, from which the strychnine will crystallize on cooling, and may be freed from adhering brucine by washing with diluted alcohol.

Commercial strychnine occurs both in the form of crystals and powder, the latter being preferred for dispensing purposes. Its taste is so intensely bitter that it is perceptible if but $\frac{1}{8}$ grain be dissolved in 10 gallons of water.

The blue color obtained when strychnine is added to a solution of potassium dichromate and sulphuric acid is due to an oxidation-product, the exact nature of which is unknown, as it has not been possible to isolate the blue compound on account of its evanescent character.

Strychnine Nitrate. $\mathbf{C_{21}H_{22}N_2O_2.HNO_3}$.—This salt may be obtained by dissolving a convenient quantity of strychnine in sufficient diluted nitric acid to form a neutral solution, which is then concentrated and allowed to crystallize. It is permanent in the air and somewhat less soluble in water than strychnine sulphate, requiring about 42 parts for solution at ordinary room-temperature. The salt should be free from brucine and correspond to all the characteristic tests for strychnine. It contains a little over 84 per cent. of strychnine, and is therefore relatively nearly 10 per cent. stronger than the sulphate.

Strychnine Sulphate. $\mathbf{(C_{21}H_{22}N_2O_2)_2H_2SO_4 + 5H_2O}$.—This salt is best prepared by dissolving the alkaloid strychnine in warm diluted sulphuric acid, avoiding an excess of the latter; if a hot saturated solution is obtained, the salt will crystallize with 5 molecules (about 10.5 per cent.) of water, as required by the Pharmacopœia. When exposed to dry air the salt effloresces, and when heated to the temperature of boiling water loses all of its water of crystallization. It contains very nearly 78 per cent. of strychnine, and should be soluble in 31 parts of water at 25° C. (77° F.); the solubility is influenced by a possible loss of water of crystallization, and hence the salt must be preserved in tightly closed vials.

Veratrine.—The substance recognized, both in the Pharmacopœia and commercially, by the name veratrine is a mixture of alkaloids obtained from cevadilla seed. The mixture of alkaloids in the seed being very complex, no attempt is made at separation in the process of extraction. The seed, having been crushed, are exhausted by repeated boiling with acidulated water and the mixed decoctions evaporated to a syrupy consistence and treated with milk of lime. The precipitate thus obtained by decomposition of the natural salts of the alkaloids with veratric acid, and consisting of crude alkaloids and extractive matter, is extracted with alcohol and the latter recovered from the resulting solution, after which the residue is digested with acetic acid in order to bring the alkaloids into solution as acetates. The last-named solution is decomposed with ammonia water in excess and the precipitate, having been washed with water, is dissolved in diluted hydrochloric or sulphuric acid, the solution decolorized with animal charcoal and again precipitated with an alkali. Finally, the precipitate of mixed alkaloids is washed with water and dried at a moderate temperature. This process has the advantage over others in avoiding the extraction of fatty and resinous matter.

The most abundant and most important alkaloid in veratrine is cevadine, $C_{32}H_{49}NO_9$, which may be crystallized from alcohol in the form of anhydrous needles. It is exceedingly toxic and very irritating to the nasal mucous membrane. A solution of cevadine in nitric acid assumes a violet color upon being warmed, which changes to scarlet-red on boiling. With cold sulphuric acid cevadine yields a yellow solution, the color, however, changing to blood-red on warming. According to Allen, the facility with which cevadine undergoes hydrolysis is the cause of the formation of much amorphous alkaloid and other products in the extraction of cevadilla seed.

Besides cevadine, veratridine, $C_{37}H_{53}NO_{11}$, named veratrine by its discoverers, Luff and Wright, is present in the official veratrine, and also cevadilline or sabadilline, $C_{34}H_{53}NO_8$, both of which are amorphous. Sabadine, $C_{29}H_{52}NO_8$, and sabadinine, $C_{37}H_{48}NO_8$, both crystallizable alkaloids, have also been found.

Owing to its intensely irritating effect upon the mucous membranes, care is necessary in handling veratrine, and dampening with alcohol or expresed oil of almond will be found desirable when mixing it with other substances. Veratrine is rarely used internally, but mostly as oleate or ointment.

Veratrine is not found in white or green hellebore, but other alkaloids, *jervine*, $C_{26}H_{37}NO_3$, and *veratroidine*, $C_{51}H_{78}N_2O_{16}$, have been isolated from these plants.

Besides the foregoing there are a number of alkaloids and alkaloidal salts not recognized in the Pharmacopœia which are of more or less interest to pharmacists, and will, therefore, be briefly considered.

Arecoline Hydrobromide. $C_8H_{13}NO_2HBr$.—This salt, which is official in the German Pharmacopœia, may be obtained by dissolving the pure alkaloid in diluted hydrobromic acid and crystallizing from an alcoholic solution. The alkaloid arecoline occurs in the areca or betel nut to the extent of 0.1 per cent., and its extraction involves a tedious and somewhat complicated process; it is the only one of the four alkaloids found in the areca nut which is highly poisonous, and, while an oily liquid of strongly basic reaction, it is soluble in water in all proportions.

Berberine. $C_{20}H_{17}NO_4$.—The chief interest attached to this alkaloid arises from the fact that, while the alkaloid is soluble in water, its salts are difficultly soluble, and are deposited in a crystalline form from acid liquids. Berberine occurs in several plants—in hydrastis to the extent of 3 or 4 per cent., from which it may be obtained by adding to a concentrated aqueous infusion of the drug hydrochloric or sulphuric acid in excess, when the corresponding berberine salt will be deposited in crystals, which, after purification by recrystallization from boiling water, may be decomposed by means of freshly prepared lead hydroxide. After filtration and concentration of the filtrate, berberine will separate as a yellow, crystalline powder.

Coniine. $C_{18}H_{17}N$.—Conium owes its medicinal virtues entirely to the volatile alkaloid, which is present in the unripe fruit (probably combined with malic acid), to the extent of 0.5 or 0.8 per cent. It can be extracted by exhausting the drug with water acidulated with acetic acid, evaporating the infusion down to an extract, in a vacuum apparatus, adding an alkali carbonate, and distilling. By collecting the distillate in diluted sulphuric acid, coniine sulphate is at once formed, which may be freed from the accompanying ammonium salt by treatment with alcohol and ether, in which the latter is insoluble; by addition of an alkali to the alcohol and ether solution and distillation, coniine will be isolated, and may be dissolved in ether, from which it can be obtained as hydrochloride, by passing dry hydrochloric acid gas into the solution, the salt being insoluble in ether. Coniine hydrochloride occurs in white crystals, which are non-deliquescent, may be dried at 100° C. (212° F.) without decomposition, and are soluble in water and alcohol.

Coniine belongs to the amines, and has been prepared synthetically by Ladenburg; it has a strong alkaline reaction and a penetrating, suffocating odor. When pure it is a colorless, oily liquid, lighter than water, and boiling at 169° C. (336.2° F.).

Narcotine. $C_{22}H_{23}NO_7$.—This substance occurs in opium, sometimes to the extent of 10 per cent. and over. Being readily soluble in chloroform and ether, it is easily extracted from powdered opium by maceration or percolation with either of these solvents, but, not being soluble in petroleum benzin, it is not removed in the present official processes for Deodorized Opium and Tincture of Deodorized Opium. Narcotine is a very weak base and does not neutralize acids; it exists in opium in a free state, and, although it forms crystallizable compounds with hydrochloric and sulphuric acids, these are readily decomposed by an excess of water, and yield narcotine to both ether and chloroform when shaken with these liquids. A solution of narcotine in sulphuric acid soon becomes yellow, and, upon heating, turns red, and finally purple.

Quinidine Sulphate. $(C_{20}H_{24}N_2O_2)_2H_2SO_4 + 2H_2O$.—Quinidine usually remains in the mother-liquors from the crystallization of quinine sulphate, from which it may be obtained by adding a large excess of ammonia water, whereby cinchonine and cinchonidine are thrown down, while quinidine remains in solution; it can subsequently be precipitated by means of caustic soda and dissolved in diluted sulphuric acid, the resulting salt being purified by recrystallization. From the purified alkaloid, obtained by precipitation with sodium hydroxide, the sulphate can be readily prepared by solution in just sufficient warm diluted sulphuric acid to neutralize the same and crystallizing; if an excess of acid be used, a salt differing from the official salt will be formed.

Quinidine sulphate somewhat resembles official quinine sulphate in appearance, and has some chemical properties in common with it, but may be distinguished by its greater solubility in water and in alcohol and by being precipitated in concentrated aqueous solution by potassium iodide. Its solutions, like those of quinine sulphate, form thalleioquin and show a blue fluorescence when acidulated with sulphuric acid.

CHAPTER LXI.

ASSAY OF ALKALOIDAL DRUGS.

In view of the fact that the Pharmacopœia demands a definite alkaloid content for seventeen crude drugs and thirty-three galenical preparations, a discussion of the subject appears desirable for the purpose of offering to students some explanation of the official and other methods in use for the quantitative determination of active principles. In the case of alkaloidal drugs the valuation may be made either gravimetrically or volumetrically, but with accuracy in the last-named case only if a single alkaloid is present, or if the exact proportion of the several alkaloids present be known.

The first step in assaying alkaloidal drugs is to extract them either with acidulated water, or with alcohol, ether, or chloroform, or a mixture of two or three of the latter-named liquids, in the presence of an alkali, usually ammonia water. In the first case the alkaloids are obtained in aqueous solution as salts of the particular acid used, while in either of the latter cases the alkaloids will be liberated by the alkali, and be dissolved as free bases in the respective solvents. If an acid solution is obtained it is transferred, either direct or after concentration to small bulk, to a glass separator, made alkaline with ammonia, or potassium or sodium hydroxide, and shaken out with chloroform or ether, or a mixture of the two solvents. If an alkaline solution, however, has been obtained, this is shaken out in a separator with successive portions of diluted acid (1, 3, or 5 per cent.), whereby the alkaloids are removed as salts in aqueous solution, which latter is then further treated as previously stated; or the alkaline solution may be evaporated to dryness and then treated with weak dilute acid, either in the cold or with aid of a gentle heat, for the purpose of getting rid of alcohol or chloroform and any fatty or resinous substances possibly held by them in solution. Some alkaloids, such as aconitine and those obtained from the mydriatic drugs, are very sensitive to heat, either alone or in the presence of strong alkalies, and hence a moderate temperature, not exceeding 50° C. (122° F.), must be employed, and sodium or potassium carbonate is to be preferred to the caustic alkalies.

As a rule, 10 or 20 Gm. of the drug in fine powder are treated with 100 or 200 Cc. of the solvent, and after due maceration (from one to six hours), with frequent agitation, an aliquot part of the fluid is withdrawn, representing a definite weight (5 or 10 Gm.) of the drug. As it is often very difficult to pour off an aliquot part of the lighter liquid entirely free from floating particles, water is added to the mixture (from 10 to 40 Cc., as may be necessary) just before the liquid is to be poured off, and the mixture actively shaken for a few minutes, which causes the powdered drug to ball together and permits the separation of a perfectly clear upper layer, easily removed by decantation.

The final solution of the alkaloids in ether or chloroform, or both, is evaporated to dryness and weighed; the weight multiplied by 100 and divided by the weight of the drug represented in the final solution will express the percentage of alkaloids in the sample of drug operated upon. If a volumetric determination is to be made, the residue of crude alkaloid is dissolved in a measured quantity of tenth-normal acid, with the aid of a moderate heat if necessary, sufficient acid being used to insure an excess, which latter is then determined by titration with fiftieth-normal alkali in the presence of a suitable indicator, either hematoxylin, cochineal, or iodeosin solution, the latter being especially intended for colored alkaloidal residues. The object of using alkali solution so much weaker than the acid is to enable the operator to approach the end of the reaction with greater precision, avoiding a large excess of alkali, and the quantity of such weaker alkali solutions used must be brought to the equivalent of the stronger acid solution by calculation. Thus, if fiftieth-normal alkali is used, 5 Cc. will be equivalent to 1 Cc. of tenth-normal acid, and hence the number of cubic centimeters necessary to neutralize the acid must be divided by 5 to find the exact number of cubic centimeters of tenth-normal acid in excess, and if this number be subtracted from the quantity of acid originally used the difference will indicate the quantity of acid neutralized by the alkaloids. Having ascertained the number of cubic centimeters of tenth-normal acid taken up by the alkaloids, the same is multiplied by the factor representing the weight of the respective pure alkaloids equivalent to one cubic centimeter to find the total quantity of alkaloid in the residue, from which the percentage of alkaloid present in the sample of drug is readily calculated as shown above.

The following list indicates the quantity of some of the leading alkaloids (anhydrous) necessary to neutralize one cubic centimeter of tenth-normal acid:

Aconitine,	0.06406 Gm.	Emetine,	0.02453 Gm.
Atropine,	0.02870 "	Hydrastine,	0.03803 "
Cephaeline,	0.02314 "	Morphine,	0.02830 "
Cinchonidine,	0.02920 "	Physostigmine,	0.02732 "
Cinchonine,	0.02920 "	Pilocarpine,	0.02066 "
Cocaine,	0.03009 "	Quinine,	0.03218 "
Coniine,	0.01262 "	Strychnine,	0.03317 "

Combined Alkaloids of Cinchona,	0.03069 Gm.
Combined Alkaloids of Ipecac,	0.02384 "

An annoying feature sometimes encountered in the shaking-out process of alkaloidal solutions is the formation of persistent emulsions, which is usually caused by too-active agitation of the contents of the separator. It may be avoided, in a large measure, by inverting the separator several times and then carefully rotating the same, without agitation, so as to cause successive fresh surfaces of the immiscible liquids to be intimately ground together, whereby the alkaloids will be transferred perfectly from one liquid to another. The use of a large volume of chloroform or ether, as the case may be, in proportion to the volume of aqueous fluid, also tends to prevent the formation of emulsions, or a small quantity of alcohol may be added to the aqueous solution before the admixture of ether or chloroform, and has proved successful in many cases, especially if the alkaloidal solution is to be evaporated to dryness and subsequently redissolved in acid water. If an emulsion has been formed, several plans may be tried to cause separation, as follows: If the alkaloidal solvent is heavier than water, more of the solvent and a small quantity of water and alcohol should be added; and if the solvent be lighter than water, sufficient sodium chloride solution may be added to cause separation. Slight emulsions are usually broken up if a glass rod be introduced as far as the bottom of the emulsion and then repeatedly twirled and slowly drawn upward. If the ethereal or chloroformic liquid is not to be evaporated subsequently, a little stearic acid fused on a piece of stiff wire may be twirled in the emulsion with good effect.

In every case of alkaloidal determination the operator must convince himself that all the alkaloid present in the sample has been extracted and that none be lost during the several steps of the process; this is best done by means of Mayer's Solution (mercuric potassium iodide test-solution), which produces with acid solutions of the alkaloids a cloudiness or precipitate, depending on the amount of alkaloid present. When this test is applied all alcohol, chloroform, or ether must be removed from the liquid before Mayer's Solution is added, otherwise the reaction will not be visible on account of the solvent effect of the substances named. The proper mode of procedure is to place a small quantity of the liquid to be tested, 0.5 or 1 Cc., in a test-tube or glass dish, and, if alkaline, make acid by the addition of sufficient dilute sulphuric acid; then warm gently to drive off any alcohol or chloroform and add a few drops of the reagent. If no cloudiness appears upon holding the tube or dish against a dark background all traces of alkaloid are absent. The test should be applied particularly when transferring alkaloids in separators from one liquid to another, as from an alkaline to an acid fluid, or vice versa, in the shaking-out process.

For the convenience of students the official methods for the assay of drugs and their preparations are here given, together with such comments as may seem desirable.

ASSAY OF ACONITE AND ITS PREPARATIONS.

The Pharmacopœia requires that when tested by the official method of assay, given below, aconite shall contain not less than 0.5 per cent. of aconitine; fluidextract of aconite, 0.4 Gm. of aconitine in 100 Cc.; tincture of aconite in 0.045 Gm. of aconitine in 100 Cc.

It must be borne in mind that aconitine is easily decomposed by application of a high heat, and hence evaporation of its solutions should be conducted at a moderate temperature. The addition of about 5 Gm. of powdered pumice to the liquid before evaporation in the three following methods, as suggested by A. B. Stevens, will be found to facilitate solution of the residue in the acid and also subsequent filtration.

Assay of Aconite.—Introduce 10 Gm. of aconite, in No. 60 powder, into a 200 Cc. Erlenmeyer flask, add 75 Cc. of a mixture of alcohol, 7 parts, and distilled water, 3 parts (by volume), stopper the flask securely, and agitate it at intervals during 4 hours. After placing a plug of cotton in the bottom of a small cylindrical glass percolator (25 Mm. in diameter), carefully transfer the contents of the flask to the percolator. When the liquid has all passed through, continue the percolation with more of the same menstruum until 150 Cc. of the percolate have been obtained. Pour the percolate into a shallow porcelain evaporating dish, and evaporate it to dryness at a temperature not exceeding 60° C. (140° F.). Add 5 Cc. of $\frac{N}{10}$ sulphuric acid solution and 10 Cc. of distilled water. When the extract is dissolved, filter the liquid into a separator, washing the dish, and filter with about 40 Cc. of distilled water. When this has passed through, add 25 Cc. of ether and 2 Cc. of ammonia water to the separator, and agitate for one minute. Draw off the lower layer into a flask, and filter the ethereal solution into a beaker. Return the contents of the flask to the separator, add 15 Cc. of ether, and agitate for one minute. Draw off the lower layer into the flask, and filter the ethereal solution into the beaker. Repeat the shaking out with two other portions of 10 Cc. each of ether. Evaporate the combined ethereal solutions to dryness, and dissolve the residue in 3 Cc. of $\frac{N}{10}$ sulphuric acid solution. Add to the solution 5 drops of hematoxylin test-solution, and then carefully run in $\frac{N}{50}$ potassium hydroxide solution until a violet color is produced, the transition stages being as follows: first yellow, then green, finally passing into violet. Divide the number of Cc. of $\frac{N}{50}$ potassium hydroxide solution used by 5, subtract this number from 3 (the 3 Cc. of $\frac{N}{10}$ acid used), multiply the remainder by 0.064, and this product by 10 (or multiply at once by 0.64), which will give the percentage of alkaloid in the aconite.

Assay of Fluidextract of Aconite.—Pour 10 Cc. of fluidextract of aconite into an evaporating dish and evaporate carefully to dryness on a water-bath at a temperature not exceeding 60° C. (140° F.).

Add 5 Cc. of $\frac{N}{10}$ sulphuric acid and 10 Cc. of distilled water. When the extract is dissolved, filter into a separator, washing the dish, and filter with about 40 Cc. of distilled water. To the contents of the separator add 25 Cc. of ether and 2 Cc. of ammonia water, and agitate for one minute. Draw off the lower layer into a flask and filter the ether into a beaker. Return the aqueous fluid to the separator, add 15 Cc. of ether, and agitate a minute. Again draw off the lower layer into the flask and filter the ether into the beaker. Repeat the process with 2 other portions of 10 Cc. each of ether. Evaporate the ether to dryness and dissolve the residue in 3 Cc. of $\frac{N}{10}$ sulphuric acid. Add to the solution 5 drops of hematoxylin test-solution, and then carefully run in $\frac{N}{50}$ potassium hydroxide solution until a violet color is produced, the transition stages being as follows: first yellow, then green, finally passing into violet. Divide the number of Cc. of $\frac{N}{50}$ potassium hydroxide solution used by 5, subtract this number from 3 (the 3 Cc. of $\frac{N}{10}$ sulphuric acid used), multiply the remainder by 0.064, and this product by 10 (or muliply at once by 0.64), which will give the weight in grammes of aconitine in 100 Cc. of the fluidextract of aconite.

Assay of Tincture of Aconite.—Transfer 100 Cc. of tincture of aconite to an evaporating dish and evaporate it carefully to dryness at a moderate temperature, and assay the resulting extract by the method given above for fluidextract of aconite, using the same details as there directed, with the exception that the multiplication of the product by 10 must be omitted; the result will represent the weight in grammes of aconitine contained in 100 Cc. of the tincture.

ASSAY OF BELLADONNA, HYOSCYAMUS, SCOPOLA AND STRAMONIUM AND THEIR PREPARATIONS.

These four mydriatic drugs containing practically the same alkaloids are tested by the same method of assay, and can therefore be considered under one general head. The Pharmacopœia makes the following requirements for the crude drugs and their preparations:

Belladonna leaves should contain not less than 0.35 per cent. of total alkaloids; belladonna plaster, not less than 0.38, nor more than 0.42, per cent.; belladonna root, not less than 0.5 per cent.; extract of belladonna leaves, 1.4 per cent.; fluidextract of belladonna root, 0.5 Gm. in 100 Cc.; tincture of belladonna leaves, 0.035 Gm. in 100 Cc.

Hyoscyamus should contain not less than 0.08 per cent. of total alkaloids; extract of hyoscyamus, 0.3 per cent.; fluidextract of hyoscyamus, 0.075 Gm. in 100 Cc.; tincture of hyoscyamus, 0.007 Gm. in 100 Cc. As hyoscyamus contains a very much smaller percentage of alkaloids than the other mydriatic drugs, a larger quantity of the drug and also of its preparations is required for assay.

Scopola should contain not less than 0.5 per cent. of total alkaloids; extract of scopola, 2 per cent.; fluidextract of scopola, 0.5 Gm. in 100 Cc.

Stramonium should contain not less than 0.35 per cent. of total alkaloids; extract of stramonium, 1.4 per cent.; fluidextract of stramonium, 0.35 Gm. in 100 Cc.; tincture of stramonium, 0.03 Gm. in 100 Cc.

Assay of Belladonna (*Leaves or Root*), **Scopola, or Stramonium.**—Place 10 Gm. of the drug, in No. 60 powder, in an Erlenmeyer flask of 100 Cc. capacity and add 50 Cc. of a mixture of chloroform 1 part, and ether 4 parts (by volume). Allow the flask to stand 10 minutes after inserting the stopper securely, then add 2 Cc. of ammonia water mixed with 3 Cc. of distilled water, and shake the flask well at frequent intervals during 1 hour. Then transfer as much as possible of the contents of the flask to a small percolator, which has been provided with a pledget of cotton packed firmly in the neck and inserted in a separator containing 6 Cc. of normal sulphuric acid diluted with 20 Cc. of distilled water. When the liquid has passed through the cotton, pack the drug firmly in the percolator with the aid of a glass rod, and having rinsed the flask with 10 Cc. of the chloroform-ether mixture, transfer the remaining contents of the flask to the percolator by the aid of several small portions (5 Cc.) of the chloroform-ether mixture, and continue the percolation with successive small portions of the same liquid (in all 50 Cc.). Next, shake the separator well for one minute, after securely inserting the stopper, and when the liquids have completely separated, draw off the acid solution into another separator. Add to the chloroform-ether mixture 10 Cc. of the sulphuric acid mixture of the same strength as that previously used, agitate well, and again draw off the acid solution into the second separator; repeat this operation once again, drawing off the acid solution as before; introduce into the acid solutions contained in the second separator a small piece of red litmus paper, then add ammonia water until the liquid is distinctly alkaline, and shake out successively with three portions (15, 15, 5 Cc.) of chloroform; collect the chloroform solutions in a beaker, place it on a water-bath containing warm water, and allow the chloroform to entirely evaporate. Dissolve the residue in 3 Cc. of ether and let this also evaporate completely. To the alkaloidal residue add 3 Cc. of $\frac{N}{10}$ sulphuric acid and 5 drops of hematoxylin test-solution (or iodeosin test-solution), then titrate the excess of acid with $\frac{N}{50}$ potassium hydroxide solution. Divide the number of cubic centimeters of $\frac{N}{50}$ potassium hydroxide solution used by 5, subtract the quotient from 3 (the 3 Cc. of $\frac{N}{10}$ sulphuric acid used), and multiply the remainder by 0.0287, and this product by 10; the result will be the percentage of total alkaloids contained in the drug.

Assay of Hyoscyamus.—The same method is employed for the assay of hyoscyamus as for the three preceding drugs, except that on account of the small yield of alkaloids, 25 Gm. of hyoscyamus are used, the quantity of chloroform-ether mixture which is added at first is increased from 50 to 100 Cc., and the product at the end of the assay is multiplied by 4 instead of 10 to find the percentage.

Assay of Belladonna Plaster.—This process is intended for the assay of belladonna plaster spread on cloth, the official plaster being made with extract of belladonna leaves, but the method is equally applicable to plasters made with extract of belladonna root or extract of scopola. Into a suitable beaker containing 50 Cc. of chloroform and 3 Cc. of ammonia water introduce 10 Gm. of the spread plaster cut into strips. Stir until the plaster is entirely removed from the cloth; then pour off the chloroform into another beaker, wash the cloth with 25 Cc. of chloroform and 1 Cc. of ammonia water carefully, and add the washings to the chloroformic solution first obtained. If necessary, repeat the washing with 25 Cc. of chloroform, and add it to the other chloroformic solutions. Then dry the cloth at a low temperature; cool and weigh it, and subtract its weight from the original weight of the plaster. To the chloroformic solution add four-fifths of its volume of alcohol, stir gently, and allow the liquid to stand until all of the rubber has separated in a compact mass. Then pour off the supernatant liquid into a separator of 250 Cc. capacity, and having prepared a solution of sulphuric acid by diluting 40 Cc. of normal sulphuric acid with 60 Cc. of distilled water, add 20 Cc. of the solution to the separator, and agitate for five minutes, rotating gently. Draw off the chloroformic solution into another separator, shake this with 10 Cc. of the sulphuric acid solution, and add the acid solution to that in the first separator. Repeat until the acid washings cease to give a reaction with mercuric potassium iodide test-solution; combine the acid liquids, and having rendered this solution alkaline with ammonia water, wash out the alkaloids with three successive portions of 25, 15, and 10 Cc. of chloroform. Collect these in a flask and distil off all the chloroform with the aid of a water-bath. To the alkaloidal residue add a slight excess of $\frac{N}{10}$ sulphuric acid, noting the quantity used, then add 10 drops of chloroform and, after rotating, evaporate the latter by means of a water-bath. Then add 5 drops of a hematoxylin test-solution and, rotating, titrate the excess of acid with $\frac{N}{50}$ potassium-hydroxide solution. Divide the number of cubic centimeters of $\frac{N}{50}$ potassium hydroxide solution used by 5, subtract the quotient from the number of cubic centimeters of $\frac{N}{10}$ sulphuric acid first added, and divide the difference by the number of grammes of belladonna plaster separated from the cloth, multiply the quotient by 0.0287, and this product by 100, which will give the percentage of mydriatic alkaloids in the belladonna plaster.

The object of adding alcohol to the chloroformic solution is to precipitate the rubber and at the same time keep the liberated alkaloids in solution. In order to insure solution of all the alkaloid, it will be found desirable to redissolve the precipitate of rubber in a fresh portion of chloroform and again treat with alcohol as before, adding the second alcoholic solution to the first.

Assay of Extract of Belladonna Leaves, of Scopola, or of Stramonium.—Weigh into a small evaporating dish 5 Gm. of extract of belladonna leaves or of stramonium, or 2 Gm. of extract of scopola, and dissolve in a mixture of alcohol 5 Cc., distilled water 10 Cc., ammonia water 2 Cc., and chloroform 20 Cc. When dissolved, transfer it to a separator, rinsing the dish with a little alcohol. Cork the separator and shake for several minutes. Draw off the chloroformic layer into a second separator, and add to the contents of the first separator 10 Cc. more of chloroform. Shake for several minutes, allow to separate, and again draw off the chloroformic layer into the second separator. Repeat this with 10 Cc. more of chloroform. To the united chloroformic solutions in the second separator add 5 Cc. of normal sulphuric acid and 10 Cc. of distilled water, and shake for several minutes. Draw off the chloroformic layer, after the liquids have separated, into a clean separator, and the aqueous fluid into a beaker, and repeat the process by adding to the chloroformic fluid 10 Cc. of distilled water and 1 Cc. of normal sulphuric acid. Draw off the chloroformic layer, rejecting the same, and then draw the acid fluid into the beaker. Filter the combined acid aqueous solutions in the beaker through a pledget of cotton into a clean separator, washing the last separator, beaker, and funnel with about 10 Cc. of distilled water. To the acid fluid in the separator add 10 Cc. of chloroform and sufficient ammonia water to produce a distinctly alkaline reaction. Shake for several minutes, and when the liquids have separated, draw off the chloroformic layer into a beaker. Repeat this process with 2 portions of 10 Cc. of each of chloroform, and evaporate the combined chloroformic liquids in the beaker to dryness on a water-bath containing warm water; dissolve the residue in 3 Cc. of ether, and allow the latter to evaporate completely. To the alkaloidal residue add 5 Cc. of $\frac{N}{10}$ sulphuric acid and 5 drops of hematoxylin test-solution, then titrate the excess of acid with $\frac{N}{50}$ potassium hydroxide solution. Divide the number of Cc. of $\frac{N}{50}$ potassium hydroxide solution used by 5, subtract the quotient from 5 (the 5 Cc. of $\frac{N}{10}$ sulphuric acid used), and multiply the remainder by 0.0287, and this product by 20, or in the case of extract of scopola by 50, to obtain the percentage of mydriatic alkaloids contained in the extract.

In the case of the extracts of belladonna leaves and stramonium, which contain a large amount of chlorophyll, it will be found almost impossible to see the lines of separation between the upper aqueous and lower chloroformic liquids, on account of the deep color of the solutions, and considerable difficulty is experienced in drawing off the lower liquid. It has been found that satisfactory results may be obtained if only 2 or 2.5 Gm., instead of 5 Gm., of the extract be used for the assay, and the method modified as follows: The 20 Cc. of chloroform having been added to the alkaline solution, the mixture shaken and allowed to stand for 15 or 20 minutes to insure complete separation, 15 Cc. of the lower liquid should be drawn off into a graduated cylinder or beaker; 10 Cc. more of chloroform are then added to the contents of the separator, and after separation 10 Cc. of the lower liquid are again drawn off into the cylinder or beaker; a second portion of 10 Cc. of chloroform is now poured into the separator, mixed with the contents and allowed to separate, when the color will be found light enough to note the line of separation sharply, and after again drawing off the lower liquid, the shaking process should be repeated once more with 10 Cc. of chloroform, so as to insure the complete removal of the alkoloids. The mixed chloroformic solutions are now treated as directed in the official process, and after the total amount of alkaloids present has been ascertained by calculation, the same must be multiplied by 100 and then divided by the weight of extract taken for the assay, in order to obtain the percentage.

There being no chlorophyll present in extract of scopola, the official method of assay will prove satisfactory, the smaller quantity of extract being directed by the Pharmacopœia on account of the larger percentage of alkaloids present. Solid extract of belladonna root may be assayed exactly like extract of scopola.

Assay of Extract of Hyoscyamus.—The method employed for the assay of this extract is identical with that given for extract of belladonna leaves, except that 10 Gm. of extract of hyoscyamus are directed to be used and the product to be multiplied by 10 instead of 20 to obtain the percentage. As the same annoyance from too much coloring matter will occur in the assay of this extract as in that of extract of belladonna leaves, and even to a large degree on account of the larger quantity of extract used, it will be found preferable to use only 5 Gm. of extract of hyoscyamus and double the quantities of chloroform directed above in the modified process for the assay of extract of belladonna leaves. The total amount of alkaloids found by calculation must then be multiplied by 20 to obtain the percentage.

Assay of Fluidextract of Belladonna Root, of Scopola, or of Stramonium.—Measure 10 Cc. of the respective fluidextract into a separator containing 10 Cc. of distilled water, 20 Cc. of chloroform, and 2 Cc. of ammonia water. Shake well for several minutes, and draw off the lower chloroformic layer into a second separator. Repeat the extraction twice with 10 Cc. of chloroform, and draw each 10 Cc. of chloroform into the second separator. To the latter add 8 Cc. of normal sulphuric acid and 20 Cc. of distilled water, shaking well for several minutes. Draw off and reject the lower chloroformic layer, and filter the acid aqueous layer into a clean separator.

Wash the last separator and filter with 10 Cc. of distilled water, adding this to the aqueous fluid in the separator. To the latter add 20 Cc. of chloroform and 4 Cc. of ammonia water, and shake well for several minutes. Draw off the lower chloroformic layer into a beaker, and repeat the extraction twice with 10 Cc. of chloroform, adding the chloroform to the beaker. Allow the chloroform in the beaker to evaporate on a moderately warm water-bath until the residue is perfectly dry. Add 5 Cc. of $\frac{N}{10}$ sulphuric acid to the beaker, and when the residual alkaloids have all dissolved, titrate the solution with $\frac{N}{50}$ potassium hydroxide solution, using 5 drops of hematoxylin or iodeosin test-solution as indicator. Divide the number of Cc. of $\frac{N}{50}$ potassium hydroxide solution used by 5, subtract the quotient from 5 (the 5 Cc. of $\frac{N}{10}$ sulphuric acid used), and multiply the remainder by 0.0287), and this product by 10 (or multiply at once by 0.287), to obtain the weight in grammes of alkaloids contained in 100 Cc. of the fluidextract.

Assay of Fluidextract of Hyoscyamus.—The method given above for the assay of the fluidextracts of belladonna root, scopola, and stramonium, may also be used for this fluidextract, except that 50 Cc. of fluidextract of hyoscyamus are directed to be used, and that the amount of total alkaloids ascertained by titration must be multiplied by 2, instead of 10, to find the quantity present in 100 Cc. In order to avoid the formation of troublesome emulsions, it will be found desirable to use at least 2½ times the quantities of chloroform directed in the assay of the preceding fluidextracts.

Assay of Tincture of Belladonna Leaves, or of Stramonium.—Transfer 100 Cc. of the respective tincture to an evaporating dish and evaporate on a water-bath until the liquid measures about 10 Cc. Add, if necessary, sufficient alcohol to dissolve any separated substance, and then assay the resulting liquid exactly in the same manner as directed for the fluidextracts of belladonna root, scopola, and stramonium, with the exception that the multiplication of the product by 10 must be omitted; the result will express the weight of alkaloids contained in 100 Cc. of the tincture.

Assay of Tincture of Hyoscyamus.—The Pharmacopœia directs this tincture to be assayed exactly in the same manner as the preceding two tinctures, but on account of the very small percentage of alkaloid in the drug, it will be found preferable to use at least 200 Cc. of the tincture, which should be evaporated to 20 Cc. and the process then continued as given for the assay of fluidextract of belladonna root. The resulting product should in that case be divided by 2 to ascertain the weight of alkaloids contained in 100 Cc. of the tincture.

ASSAY OF CINCHONA AND ITS PREPARATIONS.

The alkaloidal value of cinchona is preferably determined gravimetrically on account of the number of alkaloids present, which would cause unsatisfactory and unreliable results by the volumetric method. The Pharmacopœia requires that cinchona, as well as red cinchona, shall contain not less than 5 per cent. of anhydrous total alkaloids, and that the former shall also contain at least 4 per cent. of anhydrous ether-soluble alkaloids. It also requires that fluidextract of cinchona shall contain in 100 Cc. 4 Gm. of anhydrous ether-soluble alkaloids, and tincture of cinchona 0.75 Gm. in the same volume.

Assay of Cinchona.—Introduce 15 Gm. of cinchona, in No. 80 powder, into a flask or bottle of about 200 Cc. capacity, and add a mixture of 125 Cc. of ether and 25 Cc. of chloroform; then insert the stopper securely, shake the flask vigorously, and allow it to stand for 10 minutes. Then add 10 Cc. of ammonia water, and allow it to stand for five hours, shaking at frequent intervals (or continously with the aid of a mechanical shaker). Next add 15 Cc. of distilled water, and shake the flask vigorously for a few minutes, so as to cause the powder to settle readily on standing. When the supernatant fluid is quite clear, decant into a measuring flask, or cylinder, exactly 100 Cc. of the supernatant liquid (representing 10 Gm. of cinchona), transfer this to a separator, and add 15 Cc. of normal sulphuric acid, or sufficient to make the liquid distinctly acid. Shake the separator vigorously for one minute, and allow the two layers of liquid to separate completely. Draw off the lower aqueous layer into a flask. Then add 5 Cc. of normal sulphuric acid and 5 Cc. of distilled water to the separator, and shake it vigorously for about one minute, allow the liquids to separate as before, and again draw off the lower aqueous layer into the flask. Repeat the operation, using 5 Cc. of distilled water in the separator (without acid), drawing off the aqueous liquid into the flask. Filter the combined acid liquids into a measuring cylinder, and wash the filter and flask with enough distilled water to make the contents of the cylinder measure exactly 50 Cc. Pour half (25 Cc.) of the acid liquid into a separator marked No. 1, and the remaining half (25 Cc.) into another separator marked No. 2, which set aside.

1. *For Anhydrous Cinchona Alkaloids.*—To separator No. 1 (see above) add 25 Cc. of a mixture of chloroform 3 volumes and ether 1 volume, and add 5 Cc. of ammonia water, or sufficient to render the liquid alkaline. Insert the stopper and shake the separator carefully for three minutes, and then draw off the lower layer into a tared flask or beaker. Add 20 Cc. more of the chloroform-ether mixture to the separator, insert the stopper, and shake the liquid carefully for two minutes, again drawing off the lower layer into the tared flask. Repeat the operation with 10 Cc. of chloroform, and

draw this off into the tared flask. Reject the aqueous liquid in the separator, and with the aid of a water-bath evaporate the chloroform-ether solution in the tared flask or beaker, slowly and carefully, to dryness. Add 3 Cc. of ether to the dry residue, and again evaporate to dryness, then place the flask or beaker in an air-bath and heat at 110° C. (230° F.), until the weight after cooling remains constant. This weight in grammes multiplied by 20 will give the percentage of anhydrous total alkaloids in the cinchona.

2. *For Ether-soluble Alkaloids.*—To separator No. 2 (see above), containing the other 25 Cc. of acid liquid, add 25 Cc. of ether and 5 Cc. of ammonia water, or sufficient to render the liquid alkaline. The temperature of the liquid should be kept below 20° C. (68° F.), by cooling it, if necessary. Shake the separator moderately for two minutes, and allow the liquid to stand for ten minutes at 15° C. (59° F.); after the liquids have separated, draw off and reject the lower aqueous layer, and transfer the ethereal liquid to a tared beaker. Add 5 Cc. more of ether to the separator, rinse carefully, and add the rinsings to the liquid in the tared beaker. Evaporate the ether carefully by aid of a water-bath, dry the beaker and contents in an air-bath at 110° C. (230° F.) for 2 hours, cool and weigh. This weight in grammes, multiplied by 20, gives the percentage of the anhydrous ether-soluble alkaloids in the cinchona.

Assay of Fluidextract of Cinchona.—Measure 10 Cc. of fluidextract of cinchona into a flask or bottle of 200 Cc. capacity and pour over it a mixture of 100 Cc. of ether, 25 Cc. of chloroform, and 10 Cc. of ammonia water. Cork securely and shake vigorously for 10 minutes. Decant or pipette off 66 Cc., representing 5 Cc. of the fluidextract, into a measuring cylinder, and transfer to a separator, washing the cylinder out with 5 Cc. of ether, and adding this to the separator. Add to the latter about 10 Cc. of normal sulphuric acid, or sufficient to make the solution distinctly acid, and shake vigorously for several minutes. Draw off the lower layer into a second separator. To separator No. 1 add 5 Cc. more of normal sulphuric acid and 5 Cc. of distilled water, shake for several minutes, and when the liquids have separated draw off the lower layer into separator No. 2. Now add 5 Cc. of distilled water to separator No. 1, shake as before, and also draw off the lower aqueous layer into separator No. 2. To the contents of separator No. 2 add 25 Cc. of ether and a small piece of red litmus-paper. Then add, gradually, ammonia water, keeping the temperature of the liquids below 25° C. (77° F.), until the reaction is alkaline. Then shake vigorously for one or two minutes, and let liquids separate for ten minutes, at a temperature below 15° C. Draw off and discard the lower aqueous layer, and then transfer the ethereal layer into a tared beaker. Add 5 Cc. more of ether to the separator, rinse carefully, and add the rinsings to the tared beaker, and entirely evaporate the ether at a moderate heat on a water-bath. Then dry the beaker in an air-bath at

120° C. (248° F.) for two hours, and weigh, allowing to cool, preferably in a desiccator. Replace in the air-bath, and heat again for half an hour, cool, and weigh, repeating until the weight is constant. The weight of alkaloids so obtained multiplied by 20 gives the number of grammes of anhydrous ether-soluble alkaloids in 100 Cc. of the fluidextract.

Assay of Tincture of Cinchona.—Transfer 50 Cc. of tincture of cinchona to an evaporating dish, and evaporate it on a water-bath until it measures about 10 Cc., transfer the liquid to a bottle having the capacity of about 180 Cc., rinsing the dish with 10 Cc. of diluted alcohol, then assay the resulting liquid by the method given above for fluidextract of cinchona, with the exception that the multiplication of the product should be by 4 instead of 20; the result will represent the weight in grammes of anhydrous ether-soluble alkaloids contained in 100 Cc. of the tincture.

ASSAY OF COCA AND ITS PREPARATIONS.

Coca owes its medicinal value to the alkaloid cocaine, which is completely soluble in ether, while other alkaloids present in the drug are not at all or only slightly so, and hence the Pharmacopœia requires that coca leaves shall contain at least 0.5 per cent. of ether-soluble alkaloids, and fluidextract of coca 0.5 Gm. of the same in 100 Cc.

Assay of Coca.—Place 10 Gm. of coca, in No. 60 powder, in a flask of 100 Cc. capacity, add 50 Cc. of a mixture of chloroform 1 volume and ether 4 volumes, and insert the stopper securely. Allow the flask to stand ten minutes, then add 2 Cc. of ammonia water mixed with 3 Cc. of distilled water, and shake the flask well, at frequent intervals, during one hour. Then transfer as much as possible of the contents of the flask to a small percolator which has been provided with a pledget of cotton packed firmly in the neck, and insert in a separator containing 6 Cc. of normal sulphuric acid, diluted with 20 Cc. of distilled water. When the liquid has passed through the cotton, pack the coca firmly in the percolator with the aid of a glass rod, and, having rinsed the flask with 10 Cc. of chloroform-ether mixture, transfer the remaining contents of the flask to the percolator by the aid of several small portions (5 Cc.) of the chloroform-ether mixture, and continue the percolation with successive small portions of the same liquid (in all 50 Cc.). Next shake the separator well for one minute, after securely inserting the stopper, and when the liquids have completely separated, draw off the acid liquid into another separator. Add to the chloroform-ether mixture 10 Cc. of the sulphuric acid mixture, agitate well, and again draw off the acid liquid. Repeat this operation once again, drawing off the acid solution as before into the second separator, and introduce a small piece of red litmus-paper; then add ammonia water until the liquid is distinctly alkaline, and shake out successively with 3 portions of 25, 20, and 15 Cc. of ether. Collect the ether solutions in a beaker, place it on a water-bath filled with warm water, and allow the ether to evaporate entirely. Dissolve the residue in 3 Cc. of ether, and let this also evaporate completely. To the alkaloidal residue add 4 Cc. of $\frac{N}{10}$ sulphuric acid and 5 drops of hematoxylin or iodeosin test-solution, then titrate the excess of acid with $\frac{N}{50}$ potassium hydroxide solution. Divide the number of cubic centimeters of the $\frac{N}{50}$ potassium hydroxide solution used by 5, subtract this number from 4 (the 4 Cc. of $\frac{N}{10}$ sulphuric acid used), and multiply the remainder by 0.03, and this product by 10, to obtain the percentage of ether-soluble alkaloids contained in the coca.

Assay of Fluidextract of Coca.—Measure 10 Cc. of fluidextract of coca into a separator, add 25 Cc. of ether, and then 2 Cc. of ammonia water, shaking together for several minutes. When the fluids have separated, draw off the lower aqueous layer, into a second separator, and to this second separator add 20 Cc. more of ether, and repeat the shaking for one minute. Draw off and reject the lower aqueous layer from the second separator, and add the ethereal layer to the first separator. To this separator now add 5 Cc. of normal sulphuric acid and 5 Cc. of distilled water, shaking well for a minute or two. After the liquids have separated, draw off the lower aqueous layer into a clean separator, and repeat the extraction in the first separator with 9 Cc. of distilled water and 1 Cc. of normal sulphuric acid, shaking for a minute. Add the aqueous solution to the other separator, and reject the ether. Now add to the acid liquid 20 Cc. of ether and sufficient ammonia water to make it distinctly alkaline, and shake for a minute or two. Draw off the separated aqueous layer into another separator and the ethereal layer into a beaker. Repeat the extraction of the aqueous layer in the other separator with 15 Cc. and again with 15 Cc. of ether, and add the resulting ethereal extracts to the beaker. Now evaporate the ether from the beaker with gentle heat, and when dry add to it 5 Cc. of $\frac{N}{10}$ sulphuric acid, and stir until all the alkaloids are dissolved. Then add 5 drops of hematoxylin or iodeosin test-solution, and titrate the excess of acid with $\frac{N}{50}$ potassium hydroxide solution. Divide the number of Cc. of $\frac{N}{50}$ potassium hydroxide solution used by 5, subtract the quotient from 5 (the 5 Cc. of $\frac{N}{10}$ sulphuric acid used), and multiply the remainder by 0.03, and this product by 10 (or multiply at once by 0.3), to obtain the weight in grammes of ether-soluble alkaloids contained in 100 Cc. of the fluidextract of coca.

ASSAY OF COLCHICUM CORM AND SEED AND THEIR PREPARATIONS.

The determination of alkaloidal content in colchicum and its preparations is best made gravimetrically. The Pharmacopœia requires that colchicum corm shall contain not less than 0.35 per cent. of colchicine, and colchicum seed not less than 0.55 per cent.; also that extract of colchicum corm shall contain 1.4 per cent. of colchicine; fluidextract of colchicum seed 0.5 Gm. of colchicine in 100 Cc., and tincture of colchicum seed 0.05 Gm. in the same volume.

Assay of Colchicum Corm and Seed.—Introduce 10 Gm. of colchicum corm or seed, in No. 60 powder, into an Erlenmeyer flask of 200 Cc. capacity and add to it 100 Cc. of a mixture of 77 Cc. of ether, 25 Cc. of chloroform, 8 Cc. of alcohol, and 3 Cc. of ammonia water, insert the stopper securely, and macerate with frequent shaking for twelve hours (or preferably for four hours in a mechanical shaker). Filter a sufficient quantity of the liquid into a measuring cylinder until 50 Cc. (representing 5 Gm. of colchicum corm or seed) have been obtained; then transfer it to a beaker or dish, and evaporate it nearly to dryness by applying a very gentle heat. Dissolve the residue in 10 Cc. of ether, add 5 Cc. of water, stir well, and heat gently until the ether has evaporated. After cooling, filter the aqueous solution into a small separator, retaining the insoluble matter as much as possible in the beaker or dish. Redissolve the residue in a little ether, add 5 Cc. of water, and proceed as before. Wash the container and filter with a little water, and shake the aqueous solution well for a minute with 15 Cc. of chloroform. Draw off the chloroform, after perfect separation, into a tared flask, and again shake out the aqueous liquid with 3 portions of 10 Cc. each of chloroform, collecting these solutions in the tared flask. Evaporate the chloroform completely; dissolve the residue in a little alcohol, evaporate the latter, redissolve the residue in alcohol, evaporate the alcohol as before, and dry the residue at 100° C. (212° F.) until the weight remains constant after cooling. The weight of the residue multiplied by 20 gives the percentage of colchicine in the corm or seed.

Assay of Extract of Colchicum Corm.—Dissolve 4 Gm. of extract of colchicum corm in 20 Cc. of distilled water, carefully transfer the solution to a graduated flask, and add sufficient alcohol to make the liquid measure 100 Cc. Shake the flask well, allow it to stand five minutes, filter, and collect 50 Cc. of the filtrate (representing 2 Gm. of the extract), and evaporate it to dryness in a porcelain dish by means of a water-bath. Add to the residue 10 Cc. of ether and 5 Cc. of distilled water, stir the mixture well, and heat it gently until the ether is evaporated. After cooling, pour off the aqueous solution, filtering it into a separator, retaining as much of the insoluble matter in the dish as possible. Again treat the residue with 10 Cc. of ether and 5 Cc. of water, and proceed as before; rinse the dish and filter with a little water and collect all of the aqueous liquids in a separator. Introduce a small piece of red litmus-paper into the separator, add enough ammonia water to render the liquid alkaline, and then shake it out with three successive portions of chloroform, of 20, 15, and 10 Cc., respectively. Collect the combined chloroformic solutions in an Erlenmeyer flask, evaporate the chloroform, and add to the alkaloidal residue two successive small portions of alcohol, evaporating the alcohol each time. Now add to the residue a mixture of 5 Cc. of distilled water and 10 Cc. of ether, agitate the liquid gently and evaporate the ether, filtering the aqueous liquid into a separator. Rinse the flask with distilled water, pass the rinsings through the filter into the separator, and shake out the aqueous solution with three successive portions of chloroform, 20, 15, and 10 Cc., respectively. Collect the combined chloroformic solutions in a tared Erlenmeyer flask, evaporate the chloroform, and and treat the alkaloidal residue with two successive small portions of alcohol, evaporating the alcohol each time, and dry the residue at 100° C. (212° F.) to a constant weight. The weight multiplied by 50 will give the percentage of colchicine in the extract.

Assay of Fluidextract of Colchicum Seed.—Measure 10 Cc. of fluidextract of colchicum seed into a separator, add 1 Cc. of ammonia water, and shake out the alkaloid with 3 successive portions of 15, 15, and 10 Cc. of chloroform. Collect the chloroformic solutions in a beaker or dish, and evaporate it nearly to dryness by applying a very gentle heat. Dissolve the residue in 10 Cc. of ether, add 5 Cc. of water, stir well, and heat gently until the ether is evaporated. After cooling, filter the aqueous solution into a small separator, retaining the insoluble matter as much as possible in the beaker or dish. Redissolve the residue in a little ether, add 5 Cc. of water, and proceed as before. Wash the container and filter with a little water, and shake the aqueous solution well for one minute with 15 Cc. of chloroform. Draw off the chloroform, after perfect separation, into a tared flask, and again shake out the aqueous liquid, successively, with three portions of 10 Cc. each of chloroform, collecting these solutions in the tared flask. Evaporate the chloroform completely; dissolve the residue in a little alcohol, evaporate the latter, redissolve it in alcohol, evaporate the alcohol as before, and dry the residue at 100° C. (212 F°.) until the weight, after cooling in a desiccator, remains constant. Multiply the weight of the residue by 10, to obtain the weight in grammes of colchicine contained in 100 Cc. of the fluidextract.

Assay of Tincture of Colchicum Seed.—Transfer 100 Cc. of tincture of colchicum seed to an evaporating dish, and evaporate it on a water-bath until it measures about 10 Cc. Add, if necessary, sufficient alcohol to dissolve any separated substance, and then assay the resulting liquid by the method given above for fluidextract of colchicum seed, with the exception that the multiplication of the product by 10 be omitted; the result will represent the weight in grammes of colchicine contained in 100 Cc. of the tincture.

ASSAY OF CONIUM AND ITS PREPARATIONS.

Owing to the peculiar nature of the alkaloid coniine, it being a liquid very readily oxidized by exposure to the air, it has been found most desirable to convert it into the hydrochloride, and from the weight of the salt thus obtained to calculate the weight of pure alkaloid present in the drug. As each Gm. of coniine is capable of forming 1.286 Gm. of coniine hydrochloride, the weight of the latter multiplied by 0.777 + will represent the weight of pure alkaloid, which is the method followed in the official process of assay. The Pharmacopœia requires that conium shall contain not less than 0.5 per cent. of coniine, and fluidextract of conium 0.45 Gm. of the same alkaloid in 100 Cc. when tested by the process given below.

Assay of Conium.—Place 10 Gm. of conium, in No. 60 powder, in a 200 Cc. Erlenmeyer flask, add 100 Cc. of a mixture of ether 98 parts, alcohol 8 parts, and ammonia water 3 parts, all by volume, insert the stopper securely, and shake the flask at intervals during four hours. After the powder has settled decant 50 Cc. of the clear liquid into a beaker and add sufficient normal sulphuric acid to produce a distinctly acid reaction. Evaporate the ether at a gentle heat by the aid of a water-bath; then add 15 Cc. of alcohol, and set the beaker aside in a cool place for two hours to allow the ammonium sulphate to deposit. Filter the liquid; wash the residue and filter with a little alcohol, and add the washings to the filtrate; neutralize any excessive amount of acid with sodium carbonate test-solution, being careful to retain a slight acidity. Concentrate the liquid to 3 Cc. by the aid of a gentle heat on a water-bath, add 3 Cc. of distilled water and 2 drops of normal sulphuric acid. Add 15 Cc. of ether to remove traces of fatty matter, pour off the ether solution and repeat the washing with 15 Cc. of ether. Then transfer the acid liquid to a separator, introduce a small piece of red litmus-paper, and add sufficient sodium carbonate test-solution to render the liquid slightly alkaline; then shake out with successive portions of 15, 15, and 10 Cc. of ether. To the combined ether solutions, in a tared beaker, add, drop by drop, sufficient hydrochloric acid (5 per cent. solution) to insure an excess of acid, and then evaporate the ether by a gentle heat on a water-bath. Remove the excess of hydrochloric acid by adding to the residue 3 Cc. of alcohol, and heating gently to evaporate the liquid, repeat this operation once, and dry the residue at a temperature not exceeding 60° C. (140° F.)

until the weight, after cooling in a desiccator, remains constant. The weight of the residue multiplied by 0.777, and this product by 20, gives the percentage of coniine contained in the conium.

Assay of Fluidextract of Conium.—Transfer 10 Cc. of fluidextract of conium to an evaporating dish containing a little clean sand, and evaporate it to dryness by means of a water-bath. Mix the sand uniformly with the extract and transfer it to an Erlenmeyer flask of about 200 Cc. capacity, rinsing the dish with 100 Cc. of a mixture of ether 100 Cc., alcohol 7 Cc., and ammonia water 3 Cc., added in portions, and transfer the rinsings to the flask. Insert the stopper securely and shake the flask at intervals during 1 hour. Decant 50 Cc. of the liquid (representing 5 Cc. of the fluidextract) into a beaker, and add sufficient normal sulphuric acid to produce a distinctly acid reaction. Evaporate the ether at a gentle heat by aid of a water-bath; then add 15 Cc. of absolute alcohol, and set the beaker aside in a cool place for 2 hours to allow the ammonium sulphate to deposit. Filter the liquid; wash the residue and filter with a little absolute alcohol, and add the washings to the filtrate; neutralize any excessive amount of acid with sodium carbonate test-solution, being careful to retain a slight acidity. Concentrate the liquid to 3 Cc. by the aid of a gentle heat on a water-bath, add 3 Cc. of distilled water and 2 drops of normal sulphuric acid. Add 15 Cc. of ether to remove traces of fatty matter, pour off the ether solution, and repeat the washing. Then transfer the acid liquid to a separator, introduce a small piece of red litmus-paper, and add sufficient sodium carbonate test-solution to render the liquid slightly alkaline; then shake out with successive portions of 15, 10, and 10 Cc. of ether. To the combined ether-solutions in a tared beaker add, drop by drop, sufficient hydrochloric acid (5 per cent. solution) to insure an excess of acid, and then evaporate the ether by aid of a gentle heat on a water-bath. Remove the excess of hydrochloric acid by adding to the residue 3 Cc. of alcohol and heating gently to evaporate the liquid, repeat this operation once, and dry the residue at a temperature not exceeding 60° C. (140° F.) until the weight, after cooling in a desiccator, remains constant. Multiply the weight of the residue by 0.777, and the product by 20, to obtain the weight in grammes of coniine in 100 Cc. of the fluidextract.

ASSAY OF GUARANA AND ITS PREPARATIONS.

Since the active principles of guarana, chiefly caffeine, can be obtained in quite pure form, the Pharmacopœia directs that the assay of the drug and its preparations shall be made gravimetrically, and requires that guarana shall contain not less than 3.5 per cent. of its alkaloidal principles and fluidextract of guarana 3.5 Gm. of the same in 100 Cc.

Assay of Guarana.—Put 6 Gm. of guarana powder into a flask and pour upon it 120 Cc. of chloroform and 6 Cc. of ammonia water. Shake well at intervals for half an hour, and let stand for four hours. Pour off 100 Cc. of the liquid through a filter into a measuring cylinder, and transfer it therefrom to a flask, and distil off all the chloroform on a water-bath. Dissolve the residual alkaloids in a mixture of 2 Cc. of normal sulphuric acid and 20 Cc. of warm distilled water. Let cool and filter into a separator, rinse the beaker and filter with distilled water, add 10 Cc. of chloroform, 2 Cc. of ammonia water, and shake for a minute or two. Draw off the chloroformic solution into a tared flask and repeat the extraction three times more with 10 Cc. of chloroform, drawing each portion off into the tared flask. Distil off the chloroform, and when dry, add 2 Cc. of ether and evaporate this on a water-bath very carefully to avoid decrepitation. Dry the residue to constant weight on a water-bath and weigh. The weight found multiplied by 20 will give the percentage of alkaloids in the drug.

Assay of Fluidextract of Guarana.—Transfer to a separator 5 Cc. of fluidextract of guarana, and add 15 Cc. of chloroform and 1 Cc. of ammonia water. Shake well and allow the liquids to separate completely. Draw off the chloroform into a beaker. Shake out the fluid remaining in the separator with two additional portions of chloroform of 10 Cc. each, evaporate the combined chloroformic solutions carefully to dryness. Dissolve the alkaloidal residue in a mixture of 2 Cc. of normal sulphuric acid and 20 Cc. of warm distilled water. Allow it to cool, and filter the solution into a separator, rinse the flask and filter with distilled water, adding the rinsings to the separator, then add 20 Cc. of chloroform and 2 Cc. of ammonia water, shaking the separator for one minute. Draw off the chloroform into a tared flask, and repeat the extraction twice with 10 Cc. of chloroform, adding this to the tared flask. Distil off the chloroform, and, when dry, add 2 Cc. of ether, and evaporate this very carefully with the aid of a water-bath (to avoid decrepitation). Dry the residue to a constant weight on the water-bath. Multiply the weight by 20, which will give the weight in grammes of alkaloids contained in 100 Cc. of the fluidextract.

ASSAY OF HYDRASTIS AND ITS PREPARATIONS.

Although hydrastis contains three alkaloids, berberine, canadine, and hydrastine, the medicinal virtues of the drug seem to reside wholly in the latter, and hence the determination of its content is an excellent criterion for the valuation of the drug. The Pharmacopœia requires that hydrastis shall contain not less than 2.5 per cent. of hydrastine; fluidextract of hydrastis, 2 Gm. of hydrastine in 100 Cc. and tincture of hydrastis, 0.4 Gm. of hydrastine in 100 Cc. All three determinations are to be made gravimetrically.

Hydrastine exists in the drug partly in the free and partly in the combined state, and advantage is taken in the official method of assay of the fact that berberine is practically insoluble in ether. While hydrastine is colorless, it will be found almost impossible to obtain the alkaloid entirely free from a slight yellow color, which is due to traces of berberine.

Assay of Hydrastis.—Into a 250 Cc. flask put 15 Gm. of hydratis in No. 60 powder; add 150 Cc. of ether, shake the flask during 10 minutes, and add 5 Cc. of 10 per cent. ammonia water, shaking the flask frequently during one-half hour. Then add 15 Cc. of distilled water and shake until the drug collects in masses, and at once carefully decant 100 Cc. of the ethereal fluid, representing 10 Gm. of the drug, into a measuring-cylinder and transfer the same to a separator, rinsing the cylinder with a little ether. To the contents of the separator add 15 Cc. of normal sulphuric acid, shake moderately, and allow the liquids to separate. Draw off the lower acid solution into another separator, and to the contents of the first separator add 5 Cc. more of normal acid and 5 Cc. of distilled water and shake. After complete separation, again draw off the lower liquid into the second separator. Wash the contents of the first separator with 5 Cc. of distilled water, and after separation draw this also off into the second separator. Introduce a small piece of red litmus paper into the second separator, add 25 Cc. of ether and an excess of ammonia water, shake moderately for a few minutes and allow the liquids to separate, after which draw the lower aqueous fluid carefully into a clean separator, and pour the upper ethereal solution into a tared Erlenmeyer flask or beaker. Shake out the alkaline aqueous fluid twice more with ether, using 20 Cc. each time, and proceed as before, adding the ethereal solutions to the contents of the beaker or flask. Evaporate or distil off the ether carefully on a water-bath and dry the alkaloidal residue to constant weight at 100° C. (212° F.). The weight of dry residue found multiplied by 10 gives the percentage of hydrastine in the drug.

Assay of Fluidextract of Hydrastis.—Measure 10 Cc. of the fluidextract into a 100 Cc. measuring flask, add 85 Cc. of distilled water in which 2 Gm. of potassium iodide have been previously dissolved, and sufficient water to make 100 Cc. and shake for several minutes. Then filter off 50 Cc. of the liquid into a separator. Render the liquid alkaline with ammonia, add 30 Cc. of ether, and shake at intervals during several minutes. Draw off the aqueous layer into a beaker, and then the ethereal portion into another tared beaker. Return the aqueous solution from the beaker to the separator, and shake it with 20 Cc. more of ether for a minute. Draw off and reject the aqueous layer, and then draw off the ethereal layer into the tared beaker. Allow the ether to evaporate at a gentle heat, dry the residue in the beaker to constant weight on a water-bath, and then weigh. The weight obtained, multiplied by 20, gives the weight in grammes of hydrastine contained in 100 Cc. of the fluidextract.

The object of adding solution of potassium iodide to the fluidextract of hydrastis before rendering the latter alkaline, is to get rid of the berberine present, which is precipitated as hydroiodide and filtered out.

Assay of Tincture of Hydrastis.—Transfer 100 Cc. of tincture of hydrastis to an evaporating dish, and evaporate it on a water-bath until the liquid measures about 10 Cc. If any insoluble matter has separated, add sufficient alcohol to dissolve it, and then assay the resulting liquid by the method given above for the assay of fluidextract of hydrastis, using the same details as there directed for 10 Cc. of the fluidextract, with the exception that the weight of the residual alkaloids must be multiplied by 2 instead of by 20, as there directed, to give the weight in grammes of hydrastine contained in 100 Cc. of the tincture.

ASSAY OF IPECAC AND ITS PREPARATIONS.

The chief alkaloids found in ipecac are cephaëline and emetine or methylcephaëline, together with a very small amount of psychotrine. Although they are not always present in the same proportions, the Pharmacopœia by giving the equivalent of combined ipecac alkaloids for $\frac{N}{10}$ sulphuric acid as 0.02384 Gm. for each Cc. recognizes only the two first-named and as present in equal proportions, for the equivalent of cephaëline for the acid is 0.02314 Gm. and for emetine 0.02453 Gm., the mean of which is 0.02384 Gm. The alkaloid psychotrine, being insoluble in ether will be left in the dregs. It is possible to separate the cephaëline from the emetine by the solubility of the former in sodium hydroxide solution and then to determine the exact quantity of each present in any sample of ipecac, but for purposes of valuation of the drug this more tedious method is quite unnecessary. The official requirements are that ipecac shall contain not less than 2 per cent. of alkaloids, and the fluidextract of ipecac 1.75 Gm. of the same in 100 Cc.

Assay of Ipecac.—Introduce 15 Gm. of ipecac, in No. 80 powder, into an Erlenmeyer flask of 250 Cc. capacity, add 115 Cc. of ether and 35 Cc. of chloroform, shake the flask during five minutes, and then add 3 Cc. of ammonia water and shake the flask at intervals during half an hour. Now add 10 Cc. of distilled water, shake the liquid until the powder collects in masses, and pour off 100 Cc. of the clear ether-solution into a measuring cylinder. Transfer the latter to a separator, add 10 Cc. of normal sulphuric acid and 10 Cc. of distilled water. Shake the separator moderately during two minutes, and when the liquids have separated, draw off the lower solution into a second separator. Repeat the shaking out of the ether-solution with 3 Cc. of normal sulphuric acid and 5 Cc. of distilled water, drawing off the acid solution into the second separator. Repeat the shaking out again, using 10 Cc. of distilled water, and add the aqueous solution to the second separator. Reject the ether in the first separator, introduce a small piece of red litmus-paper into the second separator, add enough ammonia water to render the liquid alkaline, and 25 Cc. of ether, and then shake the separator vigorously during five minutes; draw off the alkaline liquid into the other separator, and the ether solution into a flask. Again shake out the alkaline liquid with 20 Cc. and 10 Cc. of ether, and, having shaken the separator during one minute, add the ether solutions to the liquid in the flask, rejecting the alkaline liquid. Distil the ether from the flask with the aid of a water-bath, and dissolve the alkaloidal residue in exactly 12 Cc. of $\frac{N}{10}$ sulphuric acid, warming gently on a water-bath if necessary. Then add 5 drops of hematoxylon test-solution and titrate with $\frac{N}{50}$ potassium hydroxide solution. Divide the number of cubic centimeters of $\frac{N}{50}$ potassium hydroxide solution used by 5, subtract the quotient from 12 (the 12 Cc. of $\frac{N}{10}$ sulphuric acid taken), and multiply the remainder by 0.0238, and this product by 10, which will give the percentage of alkaloids in the ipecac.

Assay of Fluidextract of Ipecac.—Transfer 10 Cc. of fluidextract of ipecac to a small evaporating dish, drive off the alcohol by means of a water-bath, and when almost cool add 5 Cc. of normal sulphuric acid and stir until all the alkaloids have been dissolved. Filter into a separator, rinse the dish, and wash the filter successively with 10 Cc. and 5 Cc. of distilled water, and add these liquids to the separator. To the separator add 20 Cc. of ether and a small piece of red litmus-paper; render the liquid alkaline with ammonia water, and shake for one minute. Draw off the lower aqueous layer into a beaker, and the ethereal layer into another beaker. Return the aqueous solution to the separator, and shake with 10 Cc. more of ether, adding the ethereal solution to that already in the beaker. After again returning the aqueous solution to the separator, shake again with 10 Cc. of ether, and then add the ethereal layer to that already in the beaker. Allow the combined ether solutions to evaporate either spontaneously or with the aid of a water-bath, and then add 10 Cc. of $\frac{N}{10}$ sulphuric acid. Stir the liquid carefully with a glass rod to facilitate the solution of the alkaloids, and when these have all dissolved, add 5 drops of hematoxylon solution. From a graduated burette add sufficient $\frac{N}{50}$ potassium hydroxide solution to just cause the yellow color of the solution to turn purple. Divide the number of Cc. of $\frac{N}{50}$ potassium hydroxide solution used by 5, subtract the quotient from 10 (the 10 Cc. of $\frac{N}{10}$ sulphuric acid used), and multiply the remainder by 0.0238, and this product by 10 (or multiply at once by 0.238), which will give the weight in grammes of alkaloids contained in each 100 Cc. of the fluidextract.

ASSAY OF NUX VOMICA AND ITS PREPARATIONS.

Although nux vomica contains two alkaloids in nearly the same proportions, it is preferred to determine the value of the drug and its preparations according to the strychnine content, as this alkaloid represents the chief therapeutic action of the drug and is far more poisonous than brucine. The official method of assay is somewhat tedious, but with careful manipulation will yield very satisfactory results. The Pharmacopœia requires that nux vomica shall contain not less than 1.25 per cent. of strychnine; extract of nux vomica, 5 per cent. of strychnine; fluidextract of nux vomica, 1 Gm. of strychnine in 100 Cc.; tincture of nux vomica, 0.1 Gm. of strychnine in 100 Cc.

Assay of Nux Vomica.—Introduce 20 Gm. of nux vomica, in No. 60 powder, in a 250 Cc. flask and pour over it 200 Cc. of a mixture of ether 137.5 Cc., chloroform 44 Cc., alcohol 13.5 Cc., and 10 per cent. ammonia water 5 Cc. Cork well, shake frequently during an hour, and let stand in a cool place overnight. Decant into a measuring cylinder 100 Cc. of the ethereal liquid (representing 10 Gm. of nux vomica) and pour this into a separator, preferably of globular shape. Now wash out the cylinder with a little chloroform, and add this to the separator. Next add to the contents of the latter 15 Cc. of normal sulphuric acid, and shake moderately during one minute, being careful to avoid emulsification, and after allowing the liquids to separate completely, draw off the entire acid liquid into another separator or a beaker. Repeat this treatment with 5 and 3 Cc. more of normal sulphuric acid, and after mixing all the acid solutions, pour them into a separator. If a drop of the last acid solution yields a precipitate with mercuric potassium iodide test-solution, repeat the washing of the ethereal liquid with 5 Cc. more of normal sulphuric acid. To the combined acid solutions in the separator, add a small piece of red litmus-paper, 25 Cc. of chloroform, and then an excess of ammonia water, shaking until all the alkaloids have been dissolved in the chloroform. Draw off the latter into a 100 Cc. flask, and repeat the shaking-out process with two additional portions of 15 Cc. each of chloroform, adding the latter to that already in the flask. Evaporate the combined chloroformic solutions in the flask until the alkaloidal residue is dry. Dissolve the residue in 15 Cc. of 3 per cent. sulphuric acid by the aid of water-bath heat, and cool the solution to ordinary temperature. To this solution add 3 Cc. of a previously cooled mixture of equal volumes of nitric acid (specific gravity 1.40) and distilled water, and after rotating a few times set the liquid aside for exactly ten minutes, shaking it gently three times during this interval. The resulting red liquid is transferred to a separator containing 25 Cc. of a 10 per cent. solution of sodium hydroxide, the flask being washed three times with very small quantities of distilled water, which is then added to the contents of the separator. If the liquid is not quite turbid, add 2 Cc. more of the 10 per cent. sodium hydroxide solution. Now add 20 Cc. of chloroform to the liquid in the separator, and shake well by a rotating motion for a few minutes, let separate and draw off the chloroform through a small filter, wetted with chloroform, into a beaker. Repeat this treatment twice, using 10 Cc. of chloroform each time, and draw both portions off into the beaker through the same filter. Finally, wash both filter and funnel with 5 Cc. of chloroform, and then evaporate all the chloroform on a water-bath very carefully to avoid decrepitation. To the alkaloidal residue, add 6 Cc. of $\frac{N}{10}$ sulphuric acid, 5 drops of iodeosin test-solution, about 80 Cc. of distilled water, and 20 Cc. of ether. When all the alkaloid is dissolved, titrate the excess of acid with $\frac{N}{50}$ potassium hydroxide solution until the aqueous liquid just turns pink. Divide the number of Cc. of $\frac{N}{50}$ potassium hydroxide solution used by 5, subtract this number from 6 (the 6 Cc. of $\frac{N}{10}$ sulphuric acid taken), multiply the remainder by 0.0332, and this product by 10, which will give the percentage of strychnine in the sample of nux vomica.

Assay of Extract of Nux Vomica.—Put 2 Gm. of extract of nux vomica in a beaker and dissolve it in 25 Cc. of a mixture of 16 Cc. of ether, 5 Cc. of chloroform, and 4 Cc. of ammonia water. When dissolved, transfer it to a separator, rinsing the beaker with a little chloroform, and adding the rinsings to the separator. Insert the stopper securely and shake the separator carefully for a few minutes. Draw off the aqueous layer into another separator, washing the ether solution and separator with a little water, and adding this to the second separator. Then shake out the aqueous liquid with two portions of 15 and 10 Cc., respectively, of chloroform, and add these to the first separator. If a few drops of the liquid left in the second separator still give a reaction with mercuric potassium iodide test-solution after acidulating, repeat the shaking out with 10 Cc. more of chloroform. Now shake out the chloroform solution in the first separator with three portions of 15, 10, and 10 Cc. each of sulphuric acid (3 per cent.), and collect the combined acid solutions in another separator. Introduce a small piece of red litmus-paper, add enough ammonia water to render the liquid alkaline, and extract the mixture with three portions, respectively, of 15, 10, and 10 Cc. each of chloroform. Draw off the chloroformic solutions into a beaker, and evaporate the chloroform with the aid of a water-bath. Dissolve the alkaloidal residue in the beaker in 15 Cc. of 3 per cent. sulphuric acid solution by the aid of a water-bath, and allow the liquid to cool. To this solution add 3 Cc. of a cooled mixture of equal parts of nitric acid (specific gravity 1.40) and distilled water, and after rotating the liquid a few times, set it aside for exactly ten minutes, shaking it gently three times during this interval. Transfer the resulting red liquid to a separator containing 25 Cc. of an aqueous solution of sodium hydroxide (1 in 10) and wash the beaker three times with very small amounts of distilled water, and add the washings to the separator. If the liquid be not quite turbid, add 2 Cc. more of the solution of sodium hydroxide. Now add 20 Cc. of chloroform to the separator, and shake it well by a rotating motion for a few minutes, allow the liquids to separate, and draw off the chloroform through a small filter, wetted with chloroform, into a beaker. Repeat this twice, using 10 Cc. of chloroform each time, and draw off both portions into the beaker, using the same filter. Finally, wash the filter and funnel with 5 Cc. of chloroform, and then evaporate all the chloroform by means of a water-bath, very carefully, to avoid decrepitation. To the alkaloidal residue add 10c. of $\frac{N}{10}$ sulphuric acid, 5 drops of iodeosin test-solution, about 90 Cc. of distilled water, and 20 Cc. of ether. When all the alkaloid is dissolved, titrate the excess of acid with $\frac{N}{50}$ potassium hydroxide solution until aqueous liquid just turns pink. Divide the number of Cc. of $\frac{N}{50}$ potassium hydroxide solution used by 5, subtract this number from 10 (the 10 Cc. of $\frac{N}{10}$ sulphuric acid used), multiply the remainder by 0.0332, and this product by 50, which will give the percentage of strychnine contained in the extract of nux vomica.

Assay of Fluidextract of Nux Vomica.—Transfer 10 Cc. of fluidextract of nux vomica to a porcelain dish, evaporate it to dryness by means of a water-bath, and dissolve the residue, while warm, in a mixture of 16 Cc. of ether, 5 Cc. of chloroform, and 4 Cc. of ammonia water, and transfer the solution to a separator, rinsing the dish with a little chloroform, which is to be added to the separator, and shake the separator carefully for a few minutes. When the liquids have separated, draw off the aqueous layer into another separator, washing the chloroform-ether liquid and separator with a little water, and adding this to the second separator. Then shake the aqueous liquid with two successive portions of 15 and 10 Cc., respectively, of chloroform, and add these to the first separator. If a small portion of the liquid left in the second separator still shows, after acidifying, a reaction with mercuric potassium iodide test-solution, repeat the shaking out with 10 Cc. more of chloroform. Now shake the combined liquids in the first separator with three successive portions, respectively, of 15, 10, and 10 Cc. of normal sulphuric acid, and collect the combined acid solutions in another separator. To this acid solution add a small piece of red litmus-paper and sufficient ammonia water to render it alkaline, then shake out successively with three portions, respectively, of 25, 10, and 10 Cc. of chloroform, and collect the chloroform solutions in a beaker. Evaporate the chloroform with the aid of a water-bath, dissolve the alkaloid residue in 15 Cc. of 3 per cent. sulphuric acid by the aid of a water-bath, and allow the liquid to cool. To this solution add 3 Cc. of a cooled mixture of equal volumes of nitric acid (specific gravity, 1.40) and distilled water, and, after rotating the liquid a few times, set it aside for exactly ten minutes, stirring it gently three times during this interval. Transfer the resulting red liquid to a separator containing 25 Cc. of an aqueous 10 per cent. sodium hydroxide solution, wash the beaker three times with very small amounts of distilled water, and add the washings to the separator. If the liquid is not quite turbid, add 2 Cc. more of the sodium hydroxide solution. Now add 20 Cc. of chloroform to the separator, and shake it well by a rotating motion for a few minutes, allow the liquids to separate, and draw off the chloroform through a small filter, wetted with chloroform, into a beaker. Repeat this twice, using 10 Cc. of chloroform each time, and draw off both portions into the beaker, using the same filter. Finally, wash the filter and funnel with 5 Cc. of chloroform, and then evaporate all the chloroform by means of a water-bath, very carefully, to avoid decrepitation. To the alkaloidal residue add 10 Cc. of $\frac{N}{10}$ sulphuric acid, 5 drops of iodeosin test-solution, about 80 Cc. of water, and 20 Cc. of ether. When all the alkaloid is dissolved, titrate the excess of acid with $\frac{N}{50}$ potassium hydroxide solution until the aqueous liquid just turns pink. Divide the number of Cc. of $\frac{N}{50}$ potassium hydroxide solution used by 5, subtract the quotient from 10 (the 10 Cc. of $\frac{N}{10}$ sulphuric acid used), multiply the remainder by 0.0332, and this product by 10 (or multiply at once by 0.332), which will give the weight in grammes of strychnine contained in 100 Cc. of the fluidextract of nux vomica.

Assay of Tincture of Nux Vomica.—Transfer 100 Cc. of tincture of nux vomica to a porcelain dish, evaporate to dryness on a water-bath, and assay the resulting extract by the method given on page 774 for the assay of extract of nux vomica, using the same details as there directed for 2 Gm. of the extract of nux vomica, with the exception that the multiplication by 50 be omitted; the result will represent the weight in grammes of strychnine contained in 100 Cc. of the tincture.

ASSAY OF OPIUM AND ITS PREPARATIONS.

The valuation of opium is always made on the basis of its morphine content, and the official assay method is that generally known as Squibb's method, which is a modification of that first suggested by Flücker. The Pharmacopœia demands that the morphine extracted be weighed in the form of crystals containing 1 molecule of water, about 5.9 per cent., and for this reason directs that the crystals be dried at a temperature not exceeding 60° C. (140° F.). It requires that opium in the moist state shall yield not less than 9 per cent. of crystallized morphine, and when dried and in fine or granular powder, not less than 12, and not more than 12.5, per cent. Deodorized opium should yield the same percentage of crystallized morphine as powdered opium. Extract of opium is required to yield 20 per cent. of crystallized morphine, and tincture of opium, as well as tincture of deodorized opium, must contain not less than 1.2 Gm. nor more than 1.25 Gm. of crystallizable morphine in 100 Cc. No official requirement is made for the morphine content of vinegar of opium and wine of opium, but as both preparations are directed to be made from the official powdered opium in the proportion of 10 Gm. to 100 Cc., they will, if carefully prepared, contain the same quantity of morphine as tincture of opium, or 1.2 to 1.25 Gm. in 100 Cc.

Morphine, being present in opium chiefly as sulphate, is readily extracted with water; but along with it other substances, such as codeine, narceine, coloring matter, inorganic salts, etc., are also brought into solution, which it is intended to remove entirely or retain in solution by the addition of alcohol and ether when the precipitation of morphine is finally effected. As pure morphine is not entirely insoluble in water, a dilute mother-liquid is undesirable; hence concentration of the infusion is resorted to in order to reduce the loss from this source; the addition of alcohol has been found advantageous in preventing the precipitation of much coloring matter along with the morphine, and is by no means hurtful in the proportion directed. The ether removes the codeine and other ether-soluble alkaloids, and, moreover, by its saturation of the aqueous fluid, still further reduces the solvent power of the latter on the freshly precipitated morphine. The addition of the ammonia water decomposes the morphine salt in solution, and the free alkaloid gradually separates in the form of crystals, which separation is materially aided by actively shaking the flask for ten or fifteen minutes.

As it is not always convenient to maintain a temperature at or not exceeding 60° C. (140° F.) during the drying of the crystals, this operation may be carried on in a boiling water-bath for four hours or in an air-bath at 110° C. (230° F.) for two hours, to constant weight. In this way the crystals of morphine will be rendered anhydrous, which will necessitate multiplication of the weight by 1.063, in order to get the result in terms of hydrated crystals, as demanded by the Pharmacopœia.

Assay of Opium.—Introduce 10 Gm. of opium, which, if fresh, should be in very small pieces, and if dry, in very fine powder, into an Erlenmeyer flask having a capacity of about 300 Cc., add 100 Cc. of distilled water, cork it well, and agitate every ten minutes, or in a mechanical shaker, during three hours. Then pour the whole as evenly as possible upon a wetted filter having a diameter of 12 Cm., and, when the liquid has drained off, wash the residue with distilled water, carefully dropped upon the edges of the filter and its contents, until 150 Cc. of filtrate are obtained. Then carefully transfer the moist opium back to the flask by means of a spatula, add 50 Cc. of distilled water, agitate thoroughly and repeatedly during fifteen minutes, and return the whole to the filter. When the liquid has drained off wash the residue as before, until the second filtrate measures 150 Cc., and finally collect about 20 Cc. more of a third filtrate. Evaporate in a tared capsule, first the second filtrate to a small volume, and then add the first filtrate, rinsing the vessel with the third filtrate, and continue the evaporation until the residue weighs 14 Gm.

Rotate the concentrated solution about in the capsule until the rings of extract are dissolved, pour the liquid into a tared Erlenmeyer flask having a capacity of about 100 Cc., and rinse the capsule with a few drops of water at a time, until the entire solution weighs 20 Gm. Then add 10 Gm. of alcohol, shake well, add 25 Cc. of ether, and shake again. Now add 3.5 Cc. of ammonia water from a graduated pipette or burette, stopper the flask with a sound cork, shake it thoroughly during ten minutes, and then set it aside, in a moderately cool place, for at least six hours or over night.

Remove the stopper carefully, and should any crystals adhere to it, brush them into the flask. Place in a small funnel two rapidly acting filters of a diameter of 7 Cc., plainly folded, one within the other (the triple fold of the inner filter being laid against the single side of the outer filter), wet them well with ether, and decant the ethereal solution as completely as possible upon the inner filter. Add 10 Cc. of ether to the contents of the flask, rotate it, and again decant the ethereal layer upon the inner filter. Repeat this operation with another portion of 10 Cc. of ether. Then pour the liquid in the flask into the filter, in portions, in such a way as to transfer the greater portion of the crystals to the filter, and, when the liquid has passed through, transfer the remaining crystals to the filter by washing the flask with several portions of water, using not more than about 15 Cc. in all. Use a feather or rubber-tipped glass rod to remove the crystals that adhere to the flask. Allow the double filter to drain, then apply water to the crystals, drop by drop, until they are practically free from mother-liquor, and afterward wash them, drop by drop, from a pipette, with alcohol previously saturated with powdered morphine. When this has passed through, displace the remaining alcohol by ether, using about 10 Cc. or more if necessary. Allow the filter to dry in a moderately warm place at a temperature not exceeding 60° C. (140° F.) until its weight remains constant, then carefully transfer the crystals to a tared watch-glass and weigh them.

Place the crystals (which are not quite pure) in an Erlenmeyer flask, add lime water (10 Cc. for each 0.1 Gm. of morphine), and shake the flask at intervals during half an hour. Filter through two counterpoised rapidly acting filters, one within the other, as directed above. Rinse the flask with more lime water and wash the filters with the same fluid until the filtrate, after acidulating, yields no more precipitate with mercuric potassium iodide test-solution. Press the filters until nearly dry between bibulous paper and dry them to constant weight, and weigh. Deduct the weight of the insoluble matter remaining on the filter from the weight of the impure morphine previously found. The difference multiplied by 10 represents the percentage of crystallized morphine contained in the opium.

Assay of Extract of Opium.—Dissolve 4 Gm. of extract of opium in 30 Cc. of water, filter the solution through a small filter, and wash the filter and residue with water until all soluble matters are extracted, collecting the washings separately. Evaporate, in a tared capsule, first, the washings to a small volume, then add the first filtrate, and evaporate the whole to a weight of 10 Gm. Rotate the concentrated solution about in the capsule until the rings of extract are redissolved, pour the liquid into a tared Erlenmeyer flask having a capacity of about 100 Cc., and rinse the capsule with a few drops of water at a time, until the entire solution weighs 15 Gm. Then add 7 Gm. (8.5 Cc.) of alcohol, shake well, add 20 Cc. of ether, and shake again. Now add 2.2 Cc. of ammonia water from a graduated pipette or burette, stopper the flask with a sound cork, shake it thoroughly during ten minutes, and then set it aside, in a moderately cool place, for at least six hours, or over night.

Remove the stopper carefully, and should any crystals adhere to it, brush them into the flask. Place in a small funnel two rapidly acting filters, of a diameter of 7 Gm., plainly folded, one within the other (the triple fold of the inner filter being laid against the single side of the outer filter), wet them well with ether, and decant the ethereal solution as completely as possible upon the inner filter. Add 10 Cc. of ether to the contents of the flask, rotate it, and again decant the ethereal layer upon the inner filter. Repeat this operation with another portion of 10 Cc. of ether. Then pour into the filter the liquid in the flask, in portions, in such a way as to transfer the greater portion of the crystals to the filter, and, when this has passed through, transfer the remaining crystals to the filter by washing the flask with several portions of water, using not more than about 10 Cc. in all. Allow the double filter to drain, then apply water to the crystals, drop by drop, until they are practically free from mother-water, and afterward wash them, drop by drop, from a pipette, with alcohol previously saturated with powdered morphine. When this has passed through, displace the remaining alcohol by ether, using about 10 Cc. or more if necessary. Allow the filter to dry in a moderately warm place, at a temperature not exceeding 60° C. (140° F.), until its weight remains constant, then carefully transfer the crystals to a tared watch-glass and weigh them.

Transfer the crystals (which are not quite pure) to an Erlenmeyer flask, add lime water in the proportion of 10 Cc. for each 0.1 Gm.

of morphine, and shake the flask at intervals for twenty-five minutes. Filter through two counterpoised, rapidly acting, plainly folded filters, one within the other (the triple fold of the inner filter being laid against the single fold of the outer filter). Rinse flask with more lime water and wash filter with the same fluid until filtrate, after acidulating, yields no more precipitate with Mayer's Solution. Press the filters until nearly dry between bibulous paper and dry them to constant weight, counterpoising with outer filter, and weigh. Deduct the weight of the insoluble matter on the filter from the weight of the impure morphine previously found, and the difference multiplied by 25, represents the percentage of pure crystallized morphine contained in the extract of opium.

Assay of Tincture of Opium and Tincture of Deodorized Opium.—Transfer 100 Cc. of tincture of opium or tincture of deodorized opium to an evaporating dish and evaporate it on a water-bath to about 20 Cc., add 40 Cc. of water, mix thoroughly, and set the liquid aside for one hour, occasionally stirring to disintegrate the resinous flakes adhering to the dish. Then filter the liquid and wash the filter and residue with water until all soluble matter is extracted, collecting the washings separately. Evaporate in a tared dish, first, the washings to a small volume, then add the first filtrate and evaporate the whole to a weight of 14 Gm. Determine the morphine in this extract by the method given on page 778 for the assay of opium (beginning with the word "Rotate" in the first paragraph), using the same details as there directed for 10 Gm. of opium, with the exception that the final multiplication by 10 be omitted. The result will represent the weight in grammes of crystallized morphine yielded by 100 Cc. of the tincture.

The object of evaporating the tincture to $\frac{1}{5}$ of its original bulk is to get rid of the alcohol present and thereby cause the precipitation of resinous and other matter insoluble in water. The precipitate formed must be well triturated with a glass rod to insure complete extraction of the morphine, and the filter and residue washed with water as long as the washings have a bitter taste, or when acidulated show a reaction with Mayer's Solution.

The crystallized morphine obtained from the tinctures of opium is always much purer than that obtained from opium itself, and much lighter in color.

ASSAY OF PHYSOSTIGMA AND ITS PREPARATIONS.

The chief constituent of calabar bean is physostigmine, associated with three other alkaloids of minor importance. It is soluble in ether, as is also eseridine, which acts like physostigmine, but calabarine is insoluble in that liquid. Eseramine is devoid of physiological activity. The Pharmacopœia requires that physostigma shall contain not less than 0.15 per cent. of ether-soluble alkaloids, extract of physostigma, 2 per cent., and tincture of physostigma, 0.014 Gm. of ether-soluble alkaloids in 100 Gm.

Assay of Physostigma.—Introduce 20 Gm. of physostigma, in No. 60 powder, into an Erlenmeyer flask of about 250 Cc. capacity, add 200 Cc. of ether, and shake the flask well during ten minutes. Then add 10 Cc. of an aqueous solution of sodium bicarbonate (1 in 20), and shake the mixture vigorously at intervals during four hours. Allow the powder to settle, and decant 100 Cc. of the ether-solution (representing 10 Gm. of physostigma) into a measuring cylinder; then transfer it to a separator, introduce a small piece of blue litmus-paper, and add sufficient normal sulphuric acid to render the liquid acid, and then 10 Cc. of distilled water. Shake the liquid well for several minutes, and draw off the aqueous layer into another separator. Repeat the extraction, using 2 Cc. of normal sulphuric acid and 8 Cc. of distilled water, add the acid aqueous layer to the second separator, and finally again shake out the ether solution, using 1 Cc. of normal sulphuric acid and 9 Cc. of distilled water, adding this also to the second separator. To the combined acid liquids in the second separator, add 25 Cc. of ether, a small piece of red litmus paper, and sufficient sodium bicarbonate solution (1 in 20) to render it alkaline. Shake the separator for one minute, allow the liquids to separate, and draw off the ether into a beaker. Repeat the shaking-out process with 20 Cc. and again with 15 Cc. of ether added to the separator, shake each time for one minute, allow the liquids to separate, and draw off the ether into the beaker. Carefully evaporate the ether from the combined solutions by means of a water-bath, and when dry, dissolve the residue in 5 Cc. of $\frac{N}{10}$ sulphuric acid and 20 Cc. of ether, which must be strictly neutral, and transfer this solution to a bottle, rinsing with 80 Cc. of water; add 5 drops of iodeosin test-solution, and titrate the excess of acid with $\frac{N}{50}$ potassium hydroxide until, after shaking, the aqueous liquid just acquires a pink color. Divide the number of cubic centimeters of $\frac{N}{50}$ potassium hydroxide used by 5, subtract the quotient from 5 (the 5 Cc. of $\frac{N}{10}$ sulphuric acid taken), and multiply the remainder by 0.0273, and this product by 10; the result will be the percentage of alkaloids soluble in ether contained in the drug.

Assay of Extract of Physostigma.—Put 1 Gm. of extract of physostigma into a small porcelain dish, add 5 Cc. of diluted alcohol, and digest for five minutes on a water-bath below the boiling temperature; then add about 5 Gm. of very clean, fine quartz sand, and evaporate to dryness on a water-bath, triturating thoroughly with a pestle to secure uniform admixture. When dry, carefully transfer the contents of the dish to a flask, add 100 Cc. of ether, cork well, and shake thoroughly for several minutes. Then add 20 Cc. of a 5 per cent. sodium bicarbonate solution, and shake vigorously at intervals for one hour. Let settle and decant 50 Cc. of the ethereal solution into a separator, and add 10 Cc. of distilled water and sufficient normal sulphuric acid to make the liquid acid. Shake well for one minute and draw off the aqueous layer into another separator. Repeat the extraction, using 2 Cc. each of normal sulphuric acid and 8 Cc. of distilled water, and add the acid aqueous layer to the contents of the second separator. Finally, repeat again, using 1 Cc. of normal sulphuric acid and 9 Cc. of distilled water, and draw this off also into the second separator. To the combined acid liquids in the second separator add 25 Cc. of ether and sufficient 5 per cent. sodium bicarbonate solution to make the liquid alkaline. Shake for a few minutes, let separate, and transfer the ether into a beaker. Repeat with 20 Cc., and again with 15 Cc. more of ether added to the aqueous fluid in the separator, shake for two minutes, let separate and transfer the ethereal liquid to the beaker. Evaporate the ether from the combined solutions in the beaker carefully on a water-bath, and when dry dissolve the residue in 2 Cc. of $\frac{N}{10}$ sulphuric acid; rinse the solution into a 200 Cc. flask with distilled water, add enough distilled water to bring the volume to about 90 Cc., add 25 Cc., of ether, and having shaken the flask, add 5 drops of iodeosin test-solution, then titrate the excess of acid with $\frac{N}{50}$ potassium hydroxide solution, until, after shaking, the aqueous liquid just acquires a pink color. Divide the number of Cc. of $\frac{N}{50}$ solution used by 5, subtract the quotient from 2 (the 2 Cc. of $\frac{N}{10}$ sulphuric acid taken), and multiply the remainder by 0.0273, and this product by 200; the result will be the percentage of ether-soluble alkaloids contained in the extract.

Assay of Tincture of Physostigma.—Transfer 100 Cc. of tincture of physostigma to a porcelain dish, evaporate it to dryness on a water-bath and assay the resulting extract by the method given above for the assay of extract of physostigma, using the same details as there directed for 1 Gm. of the same, with the exception that the product must be multiplied by 2 instead of 200; the result will represent the weight in grammes of ether-soluble alkaloids contained in 100 Cc. of the tincture.

ASSAY OF PILOCARPUS AND ITS PREPARATIONS.

As our knowledge of the alkaloidal constituents of jaborandi leaves, with the exception of pilocarpine, is as yet not entirely satisfactory, the Pharmacopœia very properly recognizes the valuation of the drug on the basis of total alkaloidal content as most desirable, and requires that pilocarpus shall contain not less than 0.5 per cent. of total alkaloids. This percentage represents fairly the average content of alkaloids in the leaves at the present time, for, while much inferior pilocarpus (running as low as 0.3 or 0.35 per cent. of alkaloids) is met with, it has also been possible to procure some lots containing as much as 1 per cent. and over. In the assay of pilocarpus leaves it frequently happens that persistent emulsions occur, which are difficult to break up; the addition of a little alcohol or the application of hot water to the exterior of the separator has been found to serve a good purpose. The Pharmacopœia requires that pilocarpus leaves shall contain, as already stated above, not less than 0.5 per cent. of total alkaloids, and the fluidextract of pilocarpus 0.4 Gm. of the same in 100 Cc.

Assay of Pilocarpus.—Moisten 10 Gm. of pilocarpus, in No. 60 powder, with 2 Cc. of ammonia water and 3 Cc. of chloroform, and at once pack it firmly in a small tubular percolator, the tube of which has been firmly plugged with absorbent cotton. Percolate with chloroform containing about 2 per cent. of ammonia water until the powder has been exhausted, for which purpose about 100 Cc. will usually suffice. Pour the percolate into a separator, and shake out with 15 Cc. of normal sulphuric acid, transferring the acid aqueous solution into another separator, and repeating the shaking out with 2 Cc. more of normal sulphuric acid, mixed with 8 Cc. of distilled water. Add the acid solution to the second separator, and repeat the shaking out again with 10 Cc. of distilled water, adding the aqueous liquid again to the second separator. Add 20 Cc. of chloroform to the second separator, make alkaline with ammonia water, shake well, and draw off the chloroform into a beaker. Repeat the shaking out twice with 15 Cc. and 10 Cc. of chloroform, and add the chloroform to the beaker. Evaporate the chloroform on a water-bath, and dissolve the residual alkaloids in 7 Cc. of $\frac{N}{10}$ sulphuric acid. Add 5 drops of cochineal or iodeosin test-solution, and titrate the excess of acid with $\frac{N}{50}$ potassium hydroxide solution. Divide the number of cubic centimeters of $\frac{N}{50}$ potassium hydroxide solution used by 5, subtract this number from 7 (the 7 Cc. of $\frac{N}{10}$ acid used), multiply the remainder by 0.02, and this product by 10 (or multiply at once by 0.2), which will give the percentage of total alkaloids in the drug.

Assay of Fluidextract of Pilocarpus.—Transfer 10 Cc. of fluidextract of pilocarpus to a porcelain dish containing a little clean sand, and evaporate it to dryness by means of a water-bath. Mix the sand uniformly with the extract and transfer the mixture to an Erlenmeyer flask of about 100 Cc. capacity, rinsing the dish with 25 Cc. of chloroform and 2.5 Cc. of ammonia water. Transfer the rinsings to the flask, cork it securely, and shake it well at intervals during one hour. Decant the liquid, transfer to a separator, wash the sand with several portions of chloroform, draw off and filter the chloroformic liquid into another separator. Then shake out the chloroform solution with 15 Cc. of normal sulphuric acid, drawing off the acid aqueous solution into another separator. Repeat the shaking out with a mixture of 5 Cc. of normal sulphuric acid and 5 Cc. of distilled water, collecting the acid solutions in the second separator.

Again repeat the shaking out with 10 Cc. of distilled water, and add the aqueous liquid to the second separator. Introduce into the second separator a small piece of red litmus-paper, add enough ammonia water to render the liquid alkaline, and extract the liquid with 20 Cc. of chloroform, drawing off the chloroformic solution into a beaker. Repeat the shaking out with 2 portions of 15 and 10 Cc. each of chloroform, and add the chloroformic solutions to the beaker. Evaporate the chloroform by means of a water-bath, and dissolve the alkaloidal residue in 8 Cc. of $\frac{N}{10}$ sulphuric acid. Add 5 drops of cochineal or iodeosin test-solution, and titrate the excess of acid with $\frac{N}{50}$ potassium hydroxide solution. Divide the number of Cc. of $\frac{N}{50}$ potassium hydroxide solution used by 5, subtract the quotient from 8 (the 8 Cc. of $\frac{N}{10}$ sulphuric acid used), and multiply the remainder by 0.02, and this product by 10 (or multiply at once by 0.2), to obtain the weight in grammes of alkaloids contained in 100 Cc. of the fluidextract.

CHAPTER LXII.

NEUTRAL PRINCIPLES AND GLUCOSIDES.

BESIDES organic acids and alkaloids, plants furnish a number of valuable principles which have a neutral reaction, and, for convenience, are divided into bitter principles and glucosides, the former being also known as amaroids. The distinguishing feature of the latter class is that when treated with diluted acids or ferments they split up into glucose, and a new body, differing from the original substance acted upon, but characteristic of that substance. With very few exceptions, glucosides do not contain nitrogen. Although glucosides are an important group of plant-products, only two are officially recognized in the Pharmacopœia, partly due to the fact that they do not always constitute the active principle of the plant, and are in many cases associated with other bodies. A few glucosides appear to have a dual character, for, while yielding glucose by the treatment above mentioned, some also possess basic and others acid properties. As stated in a previous chapter, both glucosides and bitter principles are distinguished from alkaloids by the ending *in* or *inum*.

The following official neutral principles are used by physicians to a greater or less extent: Aloin, chrysarobin, elaterin, glycyrrhizin, salicin, santonin, and strophanthin; of these, salicin and strophanthin are true glucosides.

Aloin.—The name aloin is used, both commercially and in the Pharmacopœia, to designate the neutral, bitter, crystalline principle of aloes, irrespective of the source, although the Pharmacopœia does state that it is chiefly prepared from Curaçao aloes.

It is more than probable that a very large proportion of the aloin sold in this country is derived from Curaçao aloes, as this variety is much richer in alóin than either Barbadoes or Socotra aloes, and, moreover, comparatively little of the latter variety reaches this market. Cape aloes, which was formerly supposed not to contain any crystalline aloin, has been shown to contain the same, and the name capaloin has been given to it. Tschirch in 1898 succeeded in crystallizing capaloin from alcohol and ether in the form of colorless needles.

Various methods have been proposed for the manufacture of aloin, the best known of which is the treatment of aloes with hot water acidulated with either hydrochloric or sulphuric acid; after the infusion has been allowed to stand for a day it is carefully decanted from sediment, concentrated at a moderate temperature, and set aside, when crystals or crystalline crusts of aloin will separate. The aloin may then be purified by recrystallization from hot water or very dilute alcohol. The addition of a little acid has been found advantageous in avoiding the contamination of aloin with non-crystallizable matter, which is less soluble in acidulated water than in plain water.

A more recent method suggested by Schaefer depends upon the property of aloin of forming very difficultly soluble compounds with the alkaline earths in ammoniacal solution, which, upon decomposition with an acid, yield aloin. The following method for determining the aloin content in aloes indicates the process of manufacture for aloin on a large scale: 50 Gm. of aloes are mixed with 300 Cc. of hot water, with the addition of a few drops of hydrochloric acid. On cooling the solution is decanted from the separated resin, mixed rapidly with 50 Cc. of 20 per cent. ammonia-water and a solution of 15 Gm. of calcium chloride in 30 Cc. of water. The precipitate is collected after fifteen minutes, the water expressed, and the lime salt decomposed by triturating it in a mortar with a slight excess of hydrochloric acid. The resulting mixture of aloin and calcium chloride is then dissolved in a small quantity of hot water, filtered, the filter washed with hot water, and the aloin crystallized out at a low temperature with the aid of ice. As much as 30 per cent. of aloin in fine, light-yellow crystals has been obtained from commercial aloes by this method.

The average yield of aloin from the different commercial varieties of aloes varies from 4 to 20 per cent. and over.

Aloin owes its value as a laxative to a substance known as emodin, with which it is associated in aloes and into which it is in all probability converted by the alkaline intestinal fluids. If aloin be treated with ether, any emodin present will be extracted, aloin being insoluble in ether. The peculiar color reactions, from orange to deep cherry-red, observed when 5 per cent. ammonia water is shaken with an ethereal extract, obtained from a decoction of aloes by agitation with ether, are due to emodin; pure aloin, freed from emodin, fails to show these colors. This is known as Borntræger's reaction and is practically identical with the official test for the limit of emodin, except that benzene is used in the latter in place of ether for solution of the emodin.

Aloin of commerce is often contaminated with resinous and other matter, which can be detected by imperfect solubility of the sample in cold water. As stated in the Pharmacopœia the aloin obtained from Curaçao aloes dissolves in nitric acid with a cherry-red color, which distinguishes it from capaloin, nataloin, and socaloin. It may also be distinguished from the two first-named by acquiring a red color by Klunge's test with copper sulphate and concentrated solution of sodium chloride; upon addition of alcohol the red color changes to violet. According to Tschirch this reaction depends upon the presence of a small percentage of isobarbaloin, and the red color will be intensified if a small quantity of hydrocyanic acid be used in place of the sodium chloride.

Chrysarobin.—This principle, derived from Goa Powder by treatment with hot benzene, is frequently confounded in commerce with chrysophanic acid. As thus obtained it is still contaminated with some impurities, but corresponds to the requirements of the Pharmacopœia; it can be obtained pure, in the form of small yellow scales, by repeated crystallization from acetic acid, and then has the composition $C_{30}H_{26}O_7$, which corresponds to the official definition. Although the Pharmacopœia states that chrysarobin is soluble in 18 parts of chloroform, the commercial article very rarely responds to this test. The following tests of the Pharmacopœia may be used to distinguish chrysarobin from chrysophanic acid, the former acquiring a violet color in both cases, while the latter produces a yellow-colored liquid: Mix 0.001 Gm. of the substance with 2 drops of nitric acid fuming and add to the red-colored mixture a few drops of ammonia water; or shake the substance for a few minutes with lime water. By oxidation chrysarobin is gradually converted into *chrysophanic acid*, $C_{15}H_{10}O_4$, which latter substance forms deep red solutions with the alkalies.

Elaterin. $C_{20}H_{28}O_5$.—Commercial elaterium owes its medicinal virtues to a neutral principle called elaterin, which may be extracted by treatment with chloroform and subsequent addition of ether to the chloroformic solution, whereby crystals of elaterin are precipitated, being practically insoluble in ether. The crystals may be further purified by washing them with a little ether and recrystallizing from chloroform. The yield of elaterin varies from 25 to 35 per cent. of the weight of elaterium, and the two substances must not be confounded with each other.

Glycyrrhizin.—This substance, although for a long time considered to be a neutral principle and also a glucoside, is now looked upon as a tribasic acid, *glycyrrhizic acid*, having the composition $C_{44}H_{63}NO_{18}$, which exists in licorice root in combination with ammonia as an acid salt. It possesses no medicinal properties, and is valuable only on account of its very sweet taste. It is recognized in the Pharmacopœia in combination with ammonia as *ammoniated glycyrrhizin*, and, in the official process for the preparation of this compound the complete extraction of glycyrrhizin from the drug is aimed at by adding ammonia water to the menstruum, so that a neutral ammonium glycyrrhizate may be formed. The addition of sulphuric acid to the percolate causes the precipitation of the glycyrrhizin, which, for the purpose of purification, is collected, redissolved in ammonia water, and again precipitated, being finally dissolved in sufficient ammonia water and obtained in scales by spreading the solution on glass and drying. When boiled with diluted sulphuric acid pure glycyrrhizin splits up into glycyrrhetin, $C_{32}H_{47}NO_4$, and parasaccharic acid, $C_6H_{10}O_8$, which latter reduces Fehling's Solution like glucose, and thus gave rise to the former view that glycerrhizin was a glucoside.

Salicin. $\mathbf{C_{13}H_{18}O_7}$.—Several methods are in use for the extraction of this principle from willow and other barks. The bark may be macerated and boiled with milk of lime, the decoction, after straining, being allowed to subside; the clear liquid is concentrated, treated with animal charcoal and evaporated to dryness, after which the residue is exhausted with weak alcohol, from which the salicin will crystallize after removal of the alcohol by distillation. Another plan is to exhaust the bark with boiling water and deprive the decoction of coloring matter and tannin by digestion with litharge or treatment with basic lead acetate; any free acid present in the liquid is neutralized with chalk. The filtrate, on concentration, will yield crystals of salicin, which may be purified by recrystallization.

When boiled with diluted sulphuric acid, salicin takes up water and splits up into glucose and saligenin or salicyl alcohol, thus, $C_{13}H_{18}O_7 + H_2O = C_6H_{12}O_6 + C_7H_8O_2$.

A characteristic reaction of salicin is the production of a bright red color when the substance is dissolved in concentrated sulphuric acid, followed by the separation of a dark red powder upon addition of water, the solution becoming colorless. The production of the fragrant odor of the oil of meadow sweet when salicin is heated with diluted sulphuric acid and potassium dichromate also serves to distinguish this substance from others; the odor is due to the formation of salicyl aldehyde.

Santonin. $\mathbf{C_{15}H_{18}O_3}$.—Chemically santonin is the anhydride of a weak acid, although generally looked upon as a neutral substance. It is obtained by mixing ground wormseed with slaked lime and exhausting the mixture with hot water; the resulting solution of calcium santoninate is concentrated and decomposed with hydrochloric acid. The crude santonin is treated with diluted ammonia water, dissolved in alcohol, and the solution decolorized with boneblack, after which it is allowed to crystallize.

Santonin possesses the property of turning yellow when exposed to the light, and then forms a yellow solution with alcohol, from which, however, it again crystallizes colorless.

The following may be mentioned as characteristic reactions of santonin: a red color is produced when 0.5 Gm. of santonin is heated with 5 Cc. of an alcoholic solution of potassium hydroxide; if 0.010 Gm. of santonin be added to a mixture of 1 Cc. each of sulphuric acid and water a colorless solution is obtained, which, when heated, assumes a violet color upon addition of one drop of ferric chloride solution.

Strophanthin.—The Pharmacopœia defines the official strophanthin to be a glucoside or mixture of glucosides obtained from strophanthus. Since strophanthus Kombé is the variety officially recognized, the glucoside must be assumed as obtained from it. Considerable confusion and uncertainty exist regarding the character of the strophanthin obtained from different species of strophanthus, and the various data published by different authors must be accepted tentatively, at least for the present.

Strophanthin may be extracted from finely powdered seed which has been previously deprived of fat by treatment with ether or petroleum benzin, with 70 per cent. alcohol. The tincture thus obtained is distilled to free it from alcohol, and the residue dissolved in water and filtered. After addition of tannic acid to the filtrate, the resulting precipitate is washed, mixed with lead oxide, dried and extracted with alcohol. The addition of ether to the alcoholic solution causes the precipitation of strophanthin.

The glucosidal character of strophanthin is shown by heating it with diluted hydrochloric acid, when strophanthidin is formed, and a sugar which reduces Fehling's Solution. Strophanthin is extremely toxic and is soluble in water and in alcohol. By heating strophanthin with dilute mineral acids, various shades of green color, changing to violet or blue, are produced, and are more or less characteristic.

Careful review by H. Thoms (1904), of the work previously done by others on the constituents of strophanthus, has shown that strophanthin obtained from the Kombé variety of seed contains small proportions of nitrogen, which were traced to the presence of choline and trigonelline, the latter alkaloids having been also found in the seed of the same variety. Strophanthin from the seed of strophanthus hispidus is free from nitrogen, but not capable of crystallization. The same author succeeded in obtaining 3.6 per cent. of crystalline strophanthin, also free from nitrogen, from the seed of strophanthus gratus, which after recrystallization was found to have the composition indicated by the formula $C_{30}H_{46}O_{12} + 9\,H_2O$. In view of the preceding statements it would seem desirable to indicate the different varieties of strophanthin according to their source, and to recognize officially the glucoside from strophanthus gratus, which has been found to possess a high therapeutic value.

Closely allied to the glucosides and neutral principles is a class of plant products, not used medicinally in a separate state, but comprising the active constituents of a number of drugs, and known by the general group name

Saponins.—The first use of the name saponin occurred in connection with the saponaceous constituent of the root of saponaria rubra, discovered in 1808 by Schrader. While formerly the view prevailed that the peculiar substance called saponin, as found in different plants, is identical, careful investigation of the subject by R. Kobert and his associates and pupils has demonstrated the fact that the name saponin should be applied to a group of plant constituents having certain chemical and physical properties in common, yet differing in constitution, physiological effect, etc.[1]

Although saponins are met with in several hundred plants, both monocotyledons and dicotyledons, distributed among 46 or more families, practically nothing is known regarding the important part they may play in plant physiology. They occur in all parts of plants; thus in the root of sarsaparilla, saponaria, senega, and helonias (chamælirium), the bulb of cyclamen, the bark of quillaja and guaiacum, the fruit of sapindus, the seed of æsculus, entada, and agrostemma, the stem of dulcamara, and the leaves of digitalis and guaiacum. Kobert inclines to the view that the saponins are formed in the leaves and deposited later in other parts of the plant.

One of the chief characteristics of the saponins, to which they owe their group name, is the property of forming aqueous solutions which foam strongly upon agitation, like solutions of soap, even when very dilute (1 in 10,000). The bubbles of froth, which in some cases are quite persistent, are destroyed if alcohol or ether be allowed to drop upon them. Another common property is the ability to hold fatty and resinous substances, when in a finely divided state, in perfect suspension in aqueous mixtures, thus producing emulsions of great stability. Finely divided vegetable substances are also kept in suspension in watery fluids by the presence of saponins. With few exceptions the saponins are readily soluble in water (all are soluble if the water be made slightly alkaline), and also in diluted alcohol, preferably if warmed. Some are soluble in cold absolute alcohol, but thus far none has been found soluble in ether, benzene, or carbon disulphide. A few dissolve with difficulty in chloroform. Many, but not all, saponins are precipitated from their solutions by addition of a saturated solution of ammonium sulphate, and this fact has been utilized as a means of separation. In some instances precipitation occurs in the cold, immediately or after the lapse of some time, while in others the application of heat is necessary, especially in weaker solutions. By this method it has been possible to separate polygalic acid from senegin in a decoction of senega, quillajic acid from quillajasapotoxin in a decoction of soap bark, and saporubric acid from saporubrin. The sapotoxin present in Levant soapwort, saponaria alba which is precipitated by ammonium sulphate, has thus been shown not to be identical with the sapotoxin in quillaja.

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[1] Due acknowledgment is hereby made of the recent very interesting and valuable publication by Professor R. Kobert, of Rostock, Germany, entitled "Beiträge zur Menntniss der Saponin Substanzen" (Contributions to our Knowledge of the Saponins), from which this brief abstract has been made.

All saponins have glucosidal properties, and are hydrolyzed when their solutions are heated with dilute mineral acids, being split up into dextrose and a non-toxic body, soluble in cold water, called sapogenin. The latter body, which is not identical for all saponins, has acid properties and forms water-soluble crystallizable salts with the alkalies. Some saponins are precipitated by neutral lead acetate others by basic lead acetate, and still others are affected by both reagents. Those precipitated by neutral lead acetate show an acid character toward litmus and Congo-red, and are designated as acids; thus, melanthinic acid, polygalic acid, quillajic acid, etc. The other saponins are neutral, some being known as sapotoxins, while others have been given specific names, such as assamin, chamælirin, senegin, etc. One drug, at least, is known to contain 3 neutral saponins —namely, sarsaparilla, the same being named parillin, sarsasaponin, and smilasaponin.

As a rule, saponins are amorphous bodies, but parillin and sarsasaponin are crystalline. They are characterized by a bitterish, acrid taste, sometimes accompanied by a burning sensation, and in fine powder are intensely irritating and sternutatory. With few exceptions saponins are decidedly toxic and have a solvent effect on red blood-corpuscles. This poisonous property prevents their use in pharmacy in many cases, where their property of permanently suspending oils and resinous matter would otherwise make it very desirable. The saponin obtained from the root of helonias dioica, and known as chamælirin, is said to have been used at times for cod-liver oil emulsions because less toxic than the saponins of quillaja bark; but inasmuch as the saponins present in guaiacum bark and leaves have been found almost entirey devoid of toxic properties, these would naturally seem preferable to all others for emulsifying purposes.

The following color reactions observed by Kobert are worthy of special note: A characteristic red coloration occurs with many saponins if they are mixed with concentrated sulphuric acid and exposed to the air for some time, or carefully warmed. With an alcoholic solution of sulphuric acid, to which a drop of dilute solution of ferric chloride has been added, a greenish-blue coloration is produced, which reaction is useful for detection of saponins in microscopic sections of vegetable drugs. A solution of selenous acid in concentrated sulphuric acid (Mecke's reagent) produces a cherry-red color with the acid saponin of cereus grandiflorus and other saponins, while a beautiful violet color is produced with guaiac-saponic acid. A very delicate reaction, resulting in an intense red color, is produced by adding to soap-bark saponins some Millon's reagent as modified by Nasse (a solution of mercuric acetate to which a drop of potassium nitrite solution has been added just before using), and warming. Kobert states that this last reaction is useful for detection of quillaja preparations in oil emulsions.

Two general formulas have been proposed to represent the composition of the saponins, $C_nH_{2n-10}O_{18}$ by Flückiger, and $C_nH_{2n-8}O_{10}$ by

Kobert, to one of which nearly all known saponins may be referred. To the first group belong quillajic acid, $C_{33}H_{56}O_{18}$, chamælirin, $C_{36}H_{62}O_{18}$, parillin (Flückiger), $C_{40}H_{70}O_{18}$, digitonin, $C_{33}H_{56}O_{18}$, sarsasaponin, $C_{40}H_{70}O_{18}$, and others, while quillajasapotoxin, $C_{17}H_{26}O_{10}$, melanthinic acid, $C_{29}H_{50}O_{10}$, senegin, $C_{18}H_{28}G_{10}$, smilasaponin, $C_{20}H_{32}O_{10}$, polygalic acid, $C_{19}H_{30}O_{10}$, and the acid and neutral saponins of guaiacum bark, $C_{21}H_{34}O_{10}$ and $C_{22}H_{36}O_{10}$, are members of the second group.

Inasmuch as the saponins are capable of forming insoluble lead compounds, Kobert recommends the following method for their extraction: To the concentrated decoction or tincture of the drug, solution of lead acetate is added; the resulting precipitate, after filtration, is mixed with some alcohol, treated with hydrogen sulphide, and again filtered. The residue is boiled with several portions of alcohol, the solutions added to the filtrate, and the whole evaporated to a syrupy consistence. Upon addition of ether to the cooled liquid, the saponins are precipitated. In order to recover any saponin not precipitable by lead acetate, solution of basic lead acetate should be added to the original filtrate, and the process then continued exactly as directed for the treatment of the precipitate obtained with neutral lead acetate.

The process of salting-out by means of ammonium sulphate may also be employed for precipitation and separation of saponins in place of the lead-acetate method mentioned above.

CHAPTER LXIII.

ANIMAL PRODUCTS USED IN PHARMACY.

BESIDES the well-known animal ferments, pancreatin and pepsin, long since introduced into medicine as valuable digestive aids, the Pharmacopœia of 1900 gives official recognition to an antitoxic serum of great value, and two very important glands of the animal body. As the pharmacist is occasionally called upon to handle these new products, it is deemed proper to give them more than a passing notice.

Antidiphtheric Serum.—The Pharmacopœia defines this preparation to be a fluid separated from the coagulated blood of a horse, immunized through the inoculation of diphtheric toxin, and directs that it should be kept in sealed glass containers, in a dark place, at a temperature between 4.5° and 15° C. (40° and 59° F.).

Although large quantities of antidiphtheric serum are now manufactured in this country, foreign products, both in the dry and liquid form, are also imported in considerable amount.

The preparation of antidiphtheric serum can only be conducted at large establishments, especially designed for that purpose, and involves three distinct steps—namely, the preparation of the toxin or diphtheric poison to be injected into the horse, the immunization of the animal, and the preparation of the antitoxin or serum officially recognized. A full and interesting account of the process may be found in the *National Standard Dispensatory*, pages 198–203.

Antidiphtheric serum is a yellowish or yellowish-brown, transparent or slightly turbid liquid, which is either odorless or has a slight odor, due to the addition of some antiseptic or preservative. It gradually loses its power, the loss varying between 10 and 30 per cent. The Pharmacopœia requires that each container should be furnished with a statement, giving the strength of the serum, expressed in antitoxic or immunity units, the name and percentage by volume of the antiseptic used for preservation of the liquid, the date when the serum was last tested, and the date beyond which it will not have the strength indicated on the statement. The standard of strength, expressed in units of antitoxic power, should be that approved or established by the United States Public Health and Marine Hospital Service at Washington, D. C.

An antitoxic or immunity unit may be defined as the amount of antitoxin which will neutralize 100 times the minimum fatal dose of a test toxin when the two are mixed together and immediately injected subcutaneously into a standard-test guinea-pig of 250 Gm. body-weight.

The antidiphtheric serum furnished by large manufacturers is put up in glass-stoppered vials or sealed glass bulbs and represents varying degrees of potency, as indicated on the label, thus 1 Cc. may contain 200, 500, 1000, 1500, 2000 or even 3000 immunity units.

While, formerly, it was necessary for American manufacturers of antidiphtheric serum to send their products to Germany for standardization, this work is now done by the Public Health and Marine Hospital Service, at its laboratory in Washington. Under an act of Congress, approved July 1, 1902, and the regulations framed thereunder, the Director of the Hygienic Laboratory is required to examine all antitoxins for purity and potency. From time to time purchases of antidiphtheric serum are made in the open market by government officials, and these are carefully examined. If found not to conform to the prescribed requirements, the manufacturer is notified and steps are taken to insure the withdrawal of that particular lot from sale. Not only is the serum tested for its potency, but great care is taken to determine its freedom from contamination by foreign bacteria, and finally to insure the absence of chemical poisons, especially tetanus toxin. The law requires all antitoxin serum to be plainly marked with the name of the article, and the address, and license number of the manufacturer.

Desiccated Suprarenal Glands.—This preparation is officially defined to be the cleaned, dried, and powdered suprarenal glands of the sheep or the ox, freed from fat.

The suprarenal capsule is situated above each kidney, and consists of an external cortex of peculiarly arranged cells derived from the mesoblast, and an internal medulla composed of cells derived originally from the sympathetic ganglia. The cortex is apparently without medicinal value, the important physiological properties residing in the medulla.

After removal of the external fat and connective tissue the glands are dried as rapidly as possible in a current of warm air at a moderate temperature, and, when sufficiently dry, are reduced to coarse powder, and the remaining fat removed by treatment with petroleum benzin. It is important that all moisture be removed, by exposure in a desiccator if necessary, in order to avoid subsequent putrefaction, after which the residue may be reduced to fine powder, and should be preserved in closely stoppered bottles.

Desiccated suprarenal glands occur as a light, yellowish-brown, amorphous powder, having a slight, characteristic odor, and partially soluble in water; 1 part represents approximately 6 parts of fresh glands, free from fat. Upon incineration it should not yield more than 7 per cent. of ash. If 0.5 Gm. of desiccated suprarenal glands be macerated with 25 Cc. of water for fifteen minutes and filtered, the filtrate should give an emerald-green color upon the addition of a few drops of ferric chloride test-solution. The green color disappears quite rapidly.

The active principle of the suprarenal glands has been isolated and found to be a basic substance, capable of combining with acids to form difficultly or non-crystallizable salts. It has been named adrenalin and epinephrin by different investigators, and occurs on the market as a light-grayish or brownish-white microcrystalline powder and also in the form of a solution of its chloride of $\frac{1}{10}$ per cent. strength. Its action is that of a powerful vasoconstrictor causing a marked rise of arterial blood-pressure, when injected intravenously.

Desiccated Thyroid Glands.—In the official definition of this preparation, the thyroid glands of sheep, which have been freed from fat and then cleaned, dried and powdered, only are recognized.

The thyroid gland is a very vascular organ, situated in front of, and on either side of, the trachea or upper windpipe. It consists of two lobes connected at their upper extremities by a bridge of pale-colored tissue. When freed from all external fat and connective tissue the lobes are broadly almond-shaped, and consist of a firm, succulent mass of tissue with dark-red color.

The preparation of powdered thyroid glands is practically the same process as mentioned in the preceding article for dried suprarenal glands, and, like these, the powder must be preserved in well-stoppered bottles to avoid absorption of moisture and subsequent deterioration.

Desiccated thyroid glands constitute a yellowish amorphous powder, having a slight peculiar odor, and partially soluble in water. It represents about five or six times its weight of the fresh glands, and upon incineration should not yield more than 6 per cent. of ash. Small proportions of iodine are present in the form of organic compounds, as shown by the official test, but iodides, added fraudulently, may be detected by treating a cold extract of the powder with sodium nitrate, and, after acidulation with strong nitric acid, shaking with chloroform.

Digestive Ferments.—It is well known that the digestion of food is of a twofold character; one takes place after the food has entered the stomach, and is called gastric or peptic digestion, the other occurring after the partly digested food leaves the stomach, is known as pancreatic or intestinal digestion. During the mastication of food it becomes mixed with the secretion of the salivary glands, which contains a substance known as *ptyalin*, belonging to the class of unorganized ferments usually termed enzymes by physiologists, from the Greek word *enzymos*, meaning fermented. The special action of ptyalin appears to be to prepare starchy food for subsequent digestion, as it is capable of converting starch into dextrose; in the presence of hydrochloric acid even as weak as 0.4 per cent., it is rendered inert, being most active in slightly alkaline liquids.

The action of ferments upon food depends upon the character of the latter, as the different ferments have specific functions and cannot be used indiscriminately for all kinds of food. Food partaken of by animals is either albuminoid or amylaceous in its nature, the former being converted into peptones, the latter into sugars. The digestive action of ferments on albuminoids is called the proteolytic action, from the word *proteolysis*, meaning the change occurring in proteids while being digested; the digestion of amylaceous food, on the other hand, is known as the amylolytic action of ferments, from *amylolysis*, meaning the conversion of starch into sugar.

The various products formed during the digestion of food are syntonin, albumoses, and peptones The first, also known as acid albumin, is probably produced by the action of hydrochloric acid (of which gastric juice contains from 0.1 to 0.25 per cent.) on albuminoid substances, and occurs soon after the ingestion of food. After peptic digestion has set in albumoses are formed, which are gradually converted into peptones, the end-products of digestion and the form in which albuminoid food is assimilated, peptones being readily diffusible and absorbed by a process of dialysis. As stated before, digestion is not completed in the stomach; the mixture of albumoses and peptones, forming a smooth, pulpy mass called chyme, passes into the intestines, where the conversion into peptones and other diffusible products is completed.

Pancreatin and pepsin are the two agents secreted in the body of all animals, without which assimilation of food would be impossible; both are recognized in the Pharmacopœia and are exceedingly interesting products.

Pancreatin.—By this name is recognized a mixture of enzymes found in the pancreatic juice, the secretion of a gland known as the pancreas, situated in the epigastric and hypochondrial regions beneath the stomach and in part next to the duodenum, with which it is connected by means of a small duct. The pancreatic juice is a clear, colorless, somewhat viscid liquid of an alkaline reaction, without odor and of an insipid, somewhat saline taste; it possesses both proteolytic and amylolytic activity, besides being capable of emulsifying fatty matter.

The Pharmacopœia gives no directions for the preparation of pancreatin, and different manufacturers probably pursue different methods. The following was suggested in the first edition of the National Formulary: Fresh pancreas of the hog, freed as much as possible from fat and adhering membranes, is reduced to a fine paste by means of a suitable mincing-machine; it is next mixed with half its weight of cold water and kneaded thoroughly and frequently during one hour, after which the mass is transferred to a strainer and forcibly expressed; the liquid is filtered as quickly as possible through flannel, and to the filtrate is added an equal volume of alcohol; the precipitate is collected, drained, and freed by pressure from as much of the adherent liquid as possible; it is then spread on shallow trays, dried by exposure to warm air at a temperature not exceeding 40° C. (104° F.) and reduced to powder. When large quantities of pancreas are operated upon it is advisable to use water saturated with chloroform, which will retard decomposition for a long time.

In some instances the finely mixed pancreas is macerated with highly diluted hydrochloric acid, in place of plain water, and the fat is often removed from the powdered mass by means of purified benzin.

Pancreatin consists of a mixture of at least 4 soluble unorganized ferments, more specifically termed enzymes, and differing from one another in their digestive functions. They are designated respectively as the proteolytic, the amylolytic, or diastasic, the fat-splitting, and the milk-curdling ferment. As yet none of the ferments has been isolated in a pure state. These enzymes do not exist as such in the cells of the pancreas, but are derived from the zymogens during the digestive process.

Trypsin, the proteolytic ferment, resembles pepsin in its behavior toward albuminoids, and continues in the intestines the work of that ferment begun in the stomach. It differs, however, from pepsin in acting best in a slightly alkaline medium and in splitting the products of peptic digestion, the albumoses and peptones, into simpler bodies, better adapted for absorption as nutritive agents. It is particularly active toward fibrin and muscular tissue, but does not digest coagulated egg-albumen as rapidly as pepsin. It also rapidly digests the casein of milk, with the intermediate formation of metacasein, coagulable by boiling. The presence of a small amount of sodium or potassium bicarbonate in the milk prevents the coagulation of the metacasein. As in the case of pepsin, the action of trypsin is confined to the surface of the substance exposed, the more soluble bodies passing into solution as fast as formed.

While the presence of about 1 per cent. of sodium carbonate or bicarbonate, of the digesting mass, is favorable to increased tryptic activity, the latter also occurs in neutral or even very slightly acid media, showing that the presence of alkali is not absolutely essential. The presence of very small proportions of acid (about 0.03 per cent. of hydrochloric or 0.25 per cent. of acetic acid) is by no means hurtful to the action of trypsin, but an increase to even as little as 0.1 per cent. of hydrochloric acid completely destroys the ferment, and hence its activity ceases at once in a medium having the degree of acidity favorable to peptic action. Trypsin is most active at a temperature between 37° and 40° C. (98.6° and 104° F.). and continues up to 50° C. (122° F.), above which it rapidly diminishes, and ceases altogether at 75° C. (167° F.).

Amylopsin, or pancreatic diastase, closely resembles ptyalin and grain diastase, both in properties and products of conversion, but its action is much more energetic, rapidly liquefying starch paste and converting starch into dextrin and maltose. Its greatest activity is manifested at a temperature between 30° and 45° C. (86° and 113° F.), and is destroyed at 65° C. (149° F.). The action of amylopsin is not increased by alkalies and is weakened by the presence of acids.

Steapson, or lipase, has the special function of emulsifying fats and splitting them up into glycerin and free fatty acids. It is rapidly destroyed by strong alcohol and by all acids, except the fatty, being the most delicate of the pancreatin enzymes. Its action on fats can be readily demonstrated by adding a few drops of a neutral solution of pancreatin to a neutral ethereal solution of butter, when upon addition of a little litmus solution the characteristic color-change will take place.

Rennin, or the milk-curdling ferment, is probably identical with that found in the stomach.

The Pharmacopœia describes pancreatin as a cream-colored, amorphous powder, possessing at most only a faint peculiar odor and a somewhat meat-like taste; slowly soluble in water, and containing not more than 10 per cent. of matter insoluble in that solvent; insoluble in alcohol. It is hygroscopic, and when exposed to the air for some time loses its value; hence it should be preserved in well-stoppered bottles. Dilution with sugar of milk seems to retard deterioration, and saccharated pancreatin has been found to retain its peptonizing value far better than the pure article. Dissolved in water, pancreatin yields a clear, pale-yellowish liquid, which is precipitated by heat, mineral acids, metallic salts, absolute glycerin, strong alcohol, and tannic acid, but not by a saturated solution of sodium chloride; in this latter respect it differs markedly from pepsin. It is not possible to prepare a solution of pancreatin which will retain the activity of all the enzymes present: this is perhaps due to the destructive effect of the trypsin upon the other ferments. Pancreatin is incompatible with acid pepsin solutions, and hence they should not be combined. In dry form the ferments of pancreatin are very stable, but in solution, neutral or alkaline, they undergo change even at ordinary temperature.

The Pharmacopœia requires that pancreatin shall convert not less than 25 times its own weight of starch into substances soluble in water; the standard of the French Pharmacopœia is over 50 per cent. higher than our own, and it is probable that the better varieties of commercial pancreatin are capable of converting 50 times their weight of starch, as shown by some samples examined. The official tests for the valuation of pancreatin, as regards both its starch-converting power and its peptonizing power, are easily applied.

Pepsin.—This ferment was discovered in 1836, by Schwann, after Eberle had furnished proof that digestion of food in the stomach is due neither to the mechanical action of the mucous membranes nor to the solvent action of acids, but is dependent upon some unorganized ferment present in the gastric juice; this ferment was determined by Schwann and named pepsin, from the Greek word *πέψις* (digestion). Pepsin is a secretory product of certain glands embedded in the tissue of the inner coating of the stomach, but has also been found in muscular tissue, urine, brain, and the mucous membrane of the intestines. True or active pepsin probably does not exist at all times in the gastric juice, but is formed by the action of hydrochloric acid and chlorides from a mother substance known as *pepsinogen*, as the digestive functions of the stomach may require; in support of this theory it has been found that glycerin will abstract increased quantities of pepsin from the mucous membrane of the stomach after this has been treated with 0.2 per cent. hydrochloric acid or 1.0 per cent. sodium chloride solution. The use of pepsin in medicine is mainly due to the efforts of Dr. Corvisart, court physician to the Emperor Napoleon III., but the quality of the commercial article has been vastly improved since that time; to the perseverance and energy of American pharmacists are due the improvements in the mode of manufacturing pepsin and the wonderful increase in digestive power of the commercial article.

In this country two kinds of pepsin are manufactured, known respectively as precipitated pepsin and soluble or scale pepsin; the former is made by the method recommended by E. Scheffer in 1872, which consists in precipitating an acid infusion (prepared cold) of clean mucous membrane of hog stomach by a saturated solution of sodium chloride, redissolving the precipitate in acid water, reprecipitating with salt in order to purify the pepsin, and finally drying at or below 40° C. (104° F.). A full account of this process may be found in the *American Journal of Pharmacy* for 1872. The process for the manufacture of the so-called scale or peptone pepsins insures an increased yield of product and higher digestive power, but not always the same degree of purity; it consists in subjecting the well-cleaned mucous membranes of animal stomachs, after being thoroughly minced by machinery, to a process of self-digestion in water acidified by hydrochloric acid at a temperature of 38°–45° C. (100.4°–113° F.), until the whole mass is converted into a uniform, transparent, glairy fluid. This is allowed to cool and deposit over night, after an addition of chloroform or sulphurous acid solution, which prevents putrefaction and in no wise interferes with the activity of the pepsin; the liquid is carefully strained, concentrated in a vacuum apparatus to a syrupy consistence, and spread upon plates of glass, where it is allowed to scale in suitable dust-free rooms. Pepsin thus prepared always contains mucus, peptones, and syntonin, while that prepared by the Scheffer method is contaminated with salt and some inert albuminous matter. In 1891 a process was patented in this country and in England, combining the advantages of the two preceding processes. The essential features are as follows: The well-cleansed and minced mucous membranes are brought to solution by digesting with acidulated water, the solution being clarified after the addition of sulphurous acid; the clear liquid is separated from the deposit and then precipitated by saturating, at a higher temperature, with sodium sulphate, whereby the pepsin is deposited, while the peptone remains in solution. The precipitated pepsin is dissolved in weak hydrochloric acid and subjected to dialysis, which removes the sodium sulphate and remaining peptones, after which the residual solution is concentrated at a low temperature and dried on plates of glass. The sodium sulphate is not lost in the process, but reclaimed from the peptone solution by recrystallization. While the U. S. Pharmacopœia recognizes only the pepsin obtained from the glandular layer of fresh hog-stomachs, and capable of digesting not less than 3000 times its own weight of freshly coagulated and disintegrated egg-albumen in six hours at a temperature of 38° to 40° C. (100.4° to 104° F.), when tested by the official process, the British Pharmacopœia admits pepsin from the stomachs of hogs, sheep, and calves, provided one part is capable of dissolving 2500 parts of hard-boiled egg-albumen at a temperature of 40.5 C. (105° F.) in the course of six hours.

French pepsin is chiefly obtained from sheep stomachs, and Boudault's preparation contains starch and sometimes lactic acid. The German Pharmacopœia does not prescribe the source of official pepsin nor the manner of its preparation; the stomachs of hogs and calves are, however, usually employed. Official German pepsin is required to dissolve 100 times its weight of hard-boiled egg-albumen in one hour, at a temperature of 45° C. (113° F.).

Pepsin exposed on a watch-glass to the air, even in damp weather, should not become sticky in the course of a few hours, showing the absence of an undue amount of peptone. It should form, with distilled water, an almost clear solution, which is not rendered turbid by the addition of acetic acid, showing the absence of mucus. (Pepsin made by Scheffer's process never yields a perfectly clear solution with water, owing to the presence of syntonin or acid albumin.) It should be free from any disagreeable or ammoniacal odor due to the presence of putrescible matter. A drop of tincture of iodine added to a solution of pepsin should not develop a blue or purplish-red color, showing the absence of starch and dextrin.

The greater the proportion of peptone present in pepsin the more rapidly does it absorb moisture from the air, and the greater the absence of mucus the less unpleasant will be the odor and the more perfectly clear will be the solution of pepsin in water, especially if the water be acidulated with acetic acid. Except in minute quantities, sodium chloride impairs the activity of pepsin; the same is true of alcohol. An aqueous solution of pepsin will decompose in a short time; after addition of hydrochloric acid it remains clear, but gradually loses its effect on albumen. Glycerin, on the other hand, preserves its virtues. Tannin and the alkali carbonates and bicarbonates inhibit the proteolytic action of pepsin. At a temperature of 63° C. (145.4° F.) the activity of pepsin is destroyed.

The mere solution of hard-boiled egg-albumen by pepsin in an acid menstruum is by no means an indication of its true value, as this can also be effected, under certain conditions, by hydrochloric acid and water alone. Complete peptonization or conversion of albumen into peptone appears to be a more positive test, but since the exact determination of peptones in a solution is only possible in the hands of the physiological chemist, the different pharmacopœias have adopted a simpler method of valuation.

Saccharated pepsin, prepared by intimately mixing one part of pepsin with nine parts of sugar of milk, is a convenient form of administering small doses of pepsin to children.

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